MINORITY WOMEN AND BREAST CANCER

HEARING

BEFORE THE

HUMAN RESOURCES AND INTERGOVERNMENTAL RELATIONS SUBCOMMITTEE

OF THE

COMMITTEE ON GOVERNMENT OPERATIONS HOUSE OF REPRESENTATIVES

ONE HUNDRED THIRD CONGRESS

SECOND SESSION

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MINORITY WOMEN AND BREAST CANCER

TUESDAY, OCTOBER 4, 1994

HOUSE OF REPRESENTATIVES,
HUMAN RESOURCES AND
INTERGOVERNMENTAL RELATIONS SUBCOMMITTEE
OF THE COMMITTEE ON GOVERNMENT OPERATIONS,
Washington, DC.

The subcommittee met, pursuant to notice, at 2:30 p.m., in room 2203, Rayburn House Office Building, Hon. Edolphus Towns (chairman of the subcommittee) presiding.

Present: Representatives Edolphus Towns and Steven Schiff.

Also present: J. Allen Hill, professional staff member; Martine M. DiCroce, clerk; and Martha B. Morgan, minority professional staff, Committee on Government Operations.

OPENING STATEMENT OF CHAIRMAN TOWNS

Mr. TOWNS. I call this hearing to order.

Today, the Subcommittee on Human Resources and Intergovernmental Relations looks at minority women and breast cancer.

Before we begin, I want to acknowledge that this is Breast Cancer Awareness Month, and welcome our visitors here today. I know that some of you are breast cancer survivors, and I want to applaud you for your courage.

Breast cancer is survivable, despite our concern today with mortality. One of the keys for survival is early detection. There is one message I know both the subcommittee and our witnesses want everyone to hear today, and that is, women should be active in consulting their physicians on the best ways to get regular screening. Don't be shy. The life you will save is your own.

A study published in the Journal of the American Medical Association last Wednesday concludes: "From this analysis, it is evident that reducing the survival disadvantage for black women with breast cancer is most likely to be achieved through strategies aimed at early recognition of disease." We should emphasize community educational efforts, improvement in access to primary care and mammography, and increased compliance with current screening recommendations.

Today, the subcommittee will hear testimony on the most important factors in the mortality differences between white women and women of color. Below age 65, black women are more than twice as likely to die from breast cancer as white women. Recent studies have considered such factors as medical insurance, types of medical care, income levels, stage of diagnosis, et cetera. We must carefully

examine these factors if we are to lower the mortality rates for all women, but especially minority women.

I want to thank our researchers for their work on these important concerns. I also thank them for taking time out from their busy schedule to be with us today.

At this time I would like to pause and recognize the gentleman from Albuquerque, New Mexico, the ranking member of this subcommittee, Mr. Schiff.

Mr. SCHIFF. Thank you, Mr. Chairman.

First I want to commend you for holding this hearing. In these last few days I cannot imagine many, if any, subjects more important than certain particular health care problems that we need to make a record of for the end of this Congress and for those who come to the next Congress.

It is my understanding, and I think you just referred to it, that women of color are struck by breast cancer at a much higher rate than Caucasian women are, which is a matter of particular concern, although of course that disease striking anyone is of course an extremely serious matter. But I am glad you are focusing in this hearing on that area to see what we can do to at least alleviate the extra impact that disease has on the minority population.

Second, I just have to say to the witnesses that if you have not had occasion to testify before Congress before, I want to say that you should not feel alarmed that most of the members of the subcommittee are not here today. This is, as you know, the last few days of the 103d Congress, and all of us have a number of things happening at the same time. I have another subcommittee meeting elsewhere that I need to also get to for a little bit.

What I want to stress, however, is that no matter how many of us individually might hear, the person you are really talking to is the gentleman making notes of what I am saying, of the testimony you are about to give, because this is recorded and this is passed on to all Members of Congress.

Thank you very much, Mr. Chairman.

I yield back.

Mr. TOWNS. Let me thank the gentleman from New Mexico for his very thoughtful statement.

At this time I would like to ask for a unanimous consent request to leave the record open for 3 days for additional opening statements from other Members.

Without objection, so moved.

[The prepared statements of Mr. Towns, Mr. Payne, and Mr. Barrett follow:]

PREPARED STATEMENT OF HON. EDOLPHUS TOWNS, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF NEW YORK

Today, the subcommittee on Human Resources and Intergovernmental Relations looks at minority women and breast cancer. Before we begin, I want to acknowledge that this is breast cancer awareness month, and welcome our visitors today. I know that some of you are breast cancer survivors, and I want to applaud your courage.

As I hope will be evident in today's hearing, breast cancer is survivable, despite our concern today with mortality. One of the keys for survival is early detection. There is one message I know that both the subcommittee and our witnesses want everyone to hear today: women should be active in consulting their physicians on the best ways to get regular screening. Do not be shy, the life you will save is your own.

A study published in the Journal of the American Medical Association last Wednesday concludes: "From this analysis, it is evident that reducing the survival disadvantage for black women with breast cancer is most likely to be achieved through strategies aimed at early recognition of disease. Future efforts should emphasize community educational efforts, improvement in access to primary care and mammography, and increased compliance with current screening recommendations."

Today, the Subcommittee will hear testimony on the most important factors in the mortality differences between white women and women of color. Below age 65, black women are more than twice as likely to die from breast cancer as white women. Recent studies have considered such factors as medical insurance, types of medical care, income levels, stage of diagnosis, et cetera. We must carefully examine these factors if we are to lower the mortality rates for all women, but especially minority women.

I hope I will not be stealing anyone's thunder by remarking that early detection is crucial to surviving with breast cancer. In keeping with the Public Health Service's role in preventing death and disease, the Centers for Disease Control has a national program for the early detection of breast and cervical cancer. Given the disparity in breast cancer mortality rates, it is especially important to increase early detection in women of color.

I want to thank our researchers for their work on these important concerns, and thank them for taking time away from that work to be here today to explain its impact to us.

PREPARED STATEMENT OF HON. DONALD M. PAYNE, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF NEW JERSEY

Good Morning. I would like to commend Chairman Towns for his leadership in calling this hearing today. I would also like to extend my regards to the panel of witnesses who have agreed to provide us with their testimony.

For most diseases, prognosis and survival for African Americans are worse than their Caucasian counterparts. These outcomes can be attributed to a number of factors, not the least of which is that African Americans generally receive inferior health care because of their generally lower socio-economic status.

Recent studies on breast cancer have indicated that delayed access to health services may not be the sole factor for increased mortality rates among African American women.

Breast cancer is the leading cause of cancer for Black women between the ages of 15 and 54 and is the number one cause of cancer deaths for Black women under 50.

However, according to Dr. Brenda K. Edwards associate director of the surveillance program at the National Cancer Institute, poor access to medical services for black women accounts for only about half of the increased death rate.

Consider that available data indicates that Black women are 2.2 times more likely to die from breast cancer than white women. The National Center for Health Statistics published evidence that shows that early detection is crucial to survival. And, if increased access to medical care does improve outcome by 50%, then its significance should not be diminished or dismissed. The survival rate for Black women is 63% compared with 78% for white women.

Furthermore, Mr. Chairman, I think it is vital that we acknowledge and examine the link between impoverished communities and the higher incidence of cancer. I concur with the U.S. Surgeon General, who said that if every criminal is entitled to an attorney, then every sick person should be entitled to a physician's care, as well.

Mr. Chairman, I would like to again commend you for your continued leadership in this important area and I look forward to hearing the testimony of our witnesses.

PREPARED STATEMENT OF HON. THOMAS M. BARRETT, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF WISCONSIN

Thank you Chairman Towns for holding this hearing today on the important matter of minority women and breast cancer. I applaud your efforts to keep minority health issues at the forefront of priorities for this Subcommittee.

Breast cancer is the most common form of cancer among American women. Great strides have been made in the fight against breast cancer and I commend all those who have served in this important battle, but survival rates are bleak for women of color. Breast cancer remains the leading cause of cancer death for African-American women.

Most who know this fact believe that the difference in mortality rates between African-American and white women is due to later-stage diagnosis of breast cancer in African-American women. The differences are commonly attributed to poverty, lack of access to care and unequal access to treatment. These obstacles are primary problems that deserve our continued attention. Recent studies, however, indicate that other factors also may be affecting minority women's breast cancer death rates.

Preliminary studies suggest the possibility of biological differences in the manifestation of breast cancer in African-American and Hispanic women compared to white women. After factoring out sociological and demographic factors, the cause of these differences remains unknown. The incidence of breast cancer may be higher in young African-Americans than young white Americans, reversing the trend found in women over the age of 45. In addition, African-American women may suffer more intransigent cancers than white women.

I am concerned that we may not be doing enough to pursue research that could confirm or negate findings of racial and ethnic differences in the manifestations of cancer. As a Congressman, my alarm stems from the fact that we could be successful in our nation's current efforts to combat breast cancer and still fail many members of our communities who continue to experience disproportionately high mortality rates.

We could succeed in our attempts to increase health care coverage and access to preventive and breast cancer treatment. We could saturate our communities with outreach programs and information. We could do it all—yet, if all of our efforts are based on one standard, a standard that may not apply to all populations of women, we have done women of color and our communities a great disservice.

Women are dying of breast cancer. Women of color are dying of breast cancer more frequently than white women. There are those who say we should not investigate and acknowledge biological differences between racial and ethnic groups. And there will always be those who will abuse scientific findings to fulfil their own agenda. But to those who say "do not ask such questions," I say, "tell that to the families of African-American women who are dying from breast cancer. Tell that to health professionals who witness groups of patients who do not respond as expected to standard therapies. Tell that to the young breast cancer patient who was previously told she was in a 'low risk' category."

We don't have time to discuss whether research focused on women of color should occur. Women are dying.

If the findings preclude generalizations for our entire nation, we should not be afraid to set out different guidelines and treatment recommendations that are appropriate for different populations. We should also make sure that our public health and medical communities are fully aware of the most recent findings. If the science is sound, I believe our society is sophisticated enough to handle the resulting complexity. Saving lives makes it worth these risks.

Again, I applaud the progress to date on breast cancer and believe that our efforts to strengthen and promote early detection and treatment must continue as the highest priority. But, when preliminary research indicates that there could be racial and ethnic differences for a disease or disorder, it is incumbent upon us to insist that comprehensive research confirms, then fully accounts for such differences.

I look forward to today's testimony and the Subcommittee's report on this hearing. The topic of this hearing is very important to me. Again, thank you Chairman Towns for providing leadership on this matter.

Mr. TOWNS. At this time I would like to call the first panel. Dr. Edward Sondik, please come forward, Acting Deputy Director of the National Cancer Institute. Dr. Brenda Edwards, also with NCI, and Dr. Michaele Christian and Dr. Otis Brawley, who will accompany them. And Ms. Rosemarie Henson, Acting Director of the Division of Cancer Prevention and Control for the Centers for Disease Control.

If you will sum up in 5 minutes, which will allow members of the committee to raise questions with you, I would appreciate it. Your entire statement will be entered in the record.

Good to see you again, Dr. Sondik.

STATEMENT OF EDWARD J. SONDIK, Ph.D., ACTING DEPUTY DIRECTOR, NATIONAL CANCER INSTITUTE, ACCOMPANIED BY BRENDA K. EDWARDS, Ph.D., ASSOCIATE DIRECTOR OF SURVEILLANCE PROGRAM; MICHAELE CHRISTIAN, HEAD, DEVELOPMENTAL CHEMOTHERAPY SECTION, INVESTIGATIONAL DRUG BRANCH; AND OTIS BRAWLEY, PROGRAM DIRECTOR, COMMUNITY ONCOLOGY AND REHABILITATION BRANCH, AND COORDINATOR, MINORITY BASED COMMUNITY CLINICAL ONCOLOGY PROGRAM

Dr. SONDIK. Thank you, Mr. Chairman.

I am Edward Sondik, Acting Deputy Director of the National Cancer Institute. I am pleased to be here with Dr. Edwards, Associate Director of the Surveillance Program, Dr. Michaele Christian, head of the Developmental Chemotherapy Section for the Investigational Drug Branch, and Dr. Otis Brawley, Program Director in the Community Oncology and Rehabilitation Branch, who also serves as the coordinator of the Minority-Based Community Clinical Oncology Program.

We thank you for providing this opportunity to discuss the very serious and compelling situation faced by African-American women who are at risk of and who develop breast cancer.

Breast cancer is indeed a critical priority for the NCI. It is the most common cancer among women, with 182,000 new cases expected this year and the second highest cause of cancer deaths behind lung cancer, with 46,000 deaths forecasted for this year.

The rate of breast cancer among minorities varies. For all minorities other than African-Americans, the burden is less than in the white population. African-Americans, however, have higher rates of death from this disease than the white population.

SEER data collected by the NCI show that the death rate for African-Americans is about 19 percent above that of white Americans. Yet the rate of new cases is on the average below that of white Americans. As part of the written testimony you have two charts which illustrate these facts as a function of age.

The rate of new cases is 19 percent below that of whites, a startling difference. The higher mortality rate reflects the fact that the survival rate, that is, the percentage of women who were alive 5 years after diagnosis with the disease, is for African-Americans considerably below that for white women: 66 percent for African-Americans versus 82 percent for white women.

The figures reflect the average burden of the disease over all ages. However, for younger African-American women, those under age 45, the rate of new cancers is above that of white women of the same age, and the death rate figures for these young women are considerably higher, as you quoted before, about double the rates for white women of the same age.

All these figures form the basis of an important research program under way at NCI to identify the reasons for the greater breast cancer burden in the African-American community. For example, research to identify the underlying factors contributing to increased incidence is under way in a study to compare African-American breast cancer patients with a demographically matched group among the white population.

Many other studies are under way as well, including: the study of the Northeast, mid-Atlantic and Long Island areas to identify reasons for the elevated rates for breast cancer in these areas; studies of the effects of pesticides among farmers and their families; and studies of what may be the different roles of the P–53 gene in African-Americans and whites, a gene implicated in a number of different cancers.

All these studies are ongoing and we don't have results yet. But a major study of the difference in survival—that is that difference between 82 percent for whites and 66 percent for African-Americans—has recently concluded, and has given us considerable information on the factors responsible for the greater mortality for African-Americans.

That study, led by Dr. Edwards and a nationwide team of investigators, was recently published in a Journal of the American Medical Association and showed that African-American women were 2.2 times more likely to die of their breast cancer than white women. The study found that approximately 40 percent of that difference is due to the later stage of the cancers diagnosed among the African-American women.

Another 18 percent is due to so-called co-morbid conditions, that is, diseases that might be present, such as diabetes and heart disease. Another 15 percent is due to the biological nature of the cancer itself, its histology and biology.

I would like to say that at least 50 percent of the survival difference can be explained by factors that, conceivably, can be changed to reduce the differential, those factors relating to early detection and access to high-quality care.

That still leaves the remaining 50 percent of the difference either unexplained or attributed to biological differences in the cancers. The differences demand and will receive continued investigation.

The implications of these differences are very important. Of primary importance, we need to redouble our efforts to ensure that African-American women participate fully in breast cancer screening programs. For women over age 50, we know from clinical trials that screening can reduce mortality by 30 percent or more.

Indeed, we believe regular screening in women age 50 and over will detect breast cancers earlier. Some expert groups recommend screening for women beginning in their 40's, while others recommend screening beginning at age 50.

The NCI is working with all these organizations to inform all women of the facts about screening so that they can make an informed decision. It is a most important point, that they be informed and make a decision with which they are comfortable.

In all of our research NCI has followed what has more recently become NIH policy, that minority groups and women be included in clinical trials unless specifically contraindicated. In general, if there is no strong evidence to indicate either the presence or the absence of a differential effect, women and minorities should be included in sufficient numbers to be able to draw valid statistical conclusions.

In our treatment studies we have been successful in recruiting representative numbers of women and African-Americans. Our studies now include some 9.8 percent African-Americans, slightly

higher than the estimated 8.6 percent, the proportion of all breast cancer cases which occur among African Americans.

We have not been as successful in our breast cancer prevention trial using tamoxifen. We are working with many groups to try to approve our accrual of African-Americans, which is now overall at about 4 percent.

It is encouraging that our most recent figures for August show that of all women who have submitted risk-assessment forms, 19 percent, well above the 4 percent figure, are African-Americans. We believe this is a result of our efforts and those of the research community to increase participation in clinical research and find ways to overcome those barriers.

We have established a separate fund to help defray the cost of the usual medical care for those women without health insurance or the financial means to obtain such care. We are also working with community groups to inform and educate women about clinical trials in general.

In addition, through such groups as the National Black Leadership Initiative on Cancer, we are identifying culturally appropriate and effective ways to promote participation in clinical trials.

We are continuing and expanding these efforts and welcome all suggestions.

To return to the reasons for the differential burden among African-Americans, the black-white survival study is an important benchmark. It allows us to concentrate our research on those areas of the greatest uncertainty, including the development of new prevention and treatment regimens, as well as the genetic and environmental causes of this major killer.

The BRCA–1 gene will enable us to better understand why young women develop breast cancer and, perhaps, to intervene to arrest that process or at least to find the disease at its earliest and most curable stages.

All of this research is for naught if the results are not effectively translated into practice. This also has been, and continues to be, a major priority for us at NCI. The National Black Leadership Initiative on Cancer, the Hispanic Leadership Initiative, the Native American Initiative, the Appalachian Initiative are all examples of our outreach efforts focused on specific populations.

For the population at large, we have a broad range of activities, including the Cancer Information Service 1–800–4–CANCER phone number for cancer, with regionally based offices tailored to the communities it serves.

Many of the programs involve NCI-supported cancer centers. For a cancer center to achieve the designation of comprehensive, it must have a community outreach component, among other programs.

We can't work alone. The control of this disease requires not only the efforts of NCI and other cancer agencies but those of the public at large. Last week a subcommittee of the National Cancer Advisory Board, the subcommittee to evaluate the national cancer program, issued a report, and I have a copy with me, called "Cancer at a Crossroads: A Report to the Nation." It calls for a renewed commitment to fund the war against cancer launched in 1971. In 1971, the Nation was confident that with a strong and sustained

financial commitment this country, a country that could conquer space could conquer this disease.

What we learned is that cancer is a much more complex problem than imagined. Sustained resources has indeed fueled an explosion of knowledge, yet cancer still presents formidable challenges. We all must work together to reduce the toll of this disease and must ensure that our research is conducted for the benefit of all Americans.

Again, I thank you for your continuing interest in the NCI, the National Cancer Program. I would be pleased to answer any questions.

[The prepared statement of Dr. Sondik follows:]

PREPARED STATEMENT OF EDWARD J. SONDIK, PH.D., ACTING DEPUTY DIRECTOR, NATIONAL CANCER INSTITUTE

INTRODUCTION

Mr. Chairman and Members of the Subcommittee, I am Edward J. Sondik, Acting Deputy Director of the National Cancer Institute (NCI), at the National Institutes of Health (NIH). Accompanying me today is Brenda K. Edwards, Associate Director of the NCI Surveillance Program. Also with me today from NCI are Dr. Michaele Christian, the Acting Chief of NCI's new Clinical Trials Monitoring Branch; and Dr. Otis Brawley, who is a Program Director in the Community Oncology and Rehabilitation Branch, and serves as coordinator of the Minority-Based Community Clinical Oncology Program. We thank you for providing us the opportunity today to discuss breast cancer in minority women.

Breast cancer is a devastating disease for all women; it does not discriminate by race, income, or ethnic background. But these factors seem to have a role in the incidence and survival patterns of the disease. To some extent, breast cancer incidence also appears to be linked to the conditions of life for modern women, such as a national tendency to eat a diet high in fat and calories and low in fruits and vegetables, and hormonal factors associated with earlier menstruation due to better nutrition, forgoing or postponing childbearing, or late menopause. Furthermore, as people age and life expectancy lengthens in our society we see higher cancer rates in general.

STATISTICS

Although much of breast cancer is curable, it is a complex disease and remains a formidable problem in our nation. It is the most frequently diagnosed cancer in American women and the second most frequent cause of cancer death in women (lung cancer is the leading cause of cancer deaths). In 1994 there will be an estimated 182,000 women diagnosed with breast cancer and 46,000 who die of the disease. It will be responsible for 32 percent of all cancers in women. The disease is particularly devastating for African American women.

To answer one of your questions, Congressman Towns, breast cancer incidence, mortality, and survival patterns differ between whites and African Americans. Age-adjusted incidence rates in white females are 19 percent higher than in African Americans (113.6 vs 95.1 cases per 100,000). However, breast cancer mortality rates in African Americans are 19 percent higher than in whites (31.9 vs 26.8 cases per 100,000). Breast cancer mortality among African American women continues to be higher than among white women, in spite of the fact that white women age 45 and over have higher incidence rates. The five-year relative survival rate for African American women diagnosed during 1983–1990 is 16 percentage points lower than that for whites (66 vs 82 five year relative rates, respectively). During the 1980s the survival differential grew wider; among cases diagnosed in the early to mid 1970s, these rates were 75 for white women and 63 for African American women. This difference was a major factor in our initiating the NCI Black/White Cancer Survival Study to identify the reasons underlying this difference.

NCI BLACK/WHITE CANCER SURVIVAL STUDY

The NCI Black/White Cancer Survival Study identified African American and white women residing in metropolitan Atlanta, New Orleans or San Francisco, newly diagnosed with primary invasive breast cancer during 1985 or 1986. Through interview, hospital and physician records, and independent pathology reviews, the

course of the disease was tracked from its earliest stages through treatment to, in some cases, death. Results showed that African American women had twice the risk of dying from breast cancer than white women during the study period. Advanced stage at diagnosis (probably due to late detection) accounted for approximately 40 percent of the two-fold difference in death rate, and another 15 percent was explained by histologic or pathologic differences in cellular makeup of the disease. Differences in treatment were not a contributing factor once stage of disease and tumor pathology were factored into the equation, but the participants' other health problems and sociodemographic factors that may be related to access and health care quality, reduced the difference in survival another 18 percent. After adjusting for all the variables, African American women experience a 30 percent higher risk of dying from the disease.

Comparative data on breast cancer rates for other minority women (e.g., Hispanics, Native Americans, Japanese, Chinese, etc.) are being developed for publication in mid-1995. Published data from the Surveillance, Epidemiology and End Results (SEER) New Mexico population-based cancer registry reports breast cancer incidence and mortality rates for New Mexico's non-Hispanic white women are comparable to those for white women nationwide. In contrast, American Indian women have extremely low incidence and mortality rates for breast cancer but their survival figures are among the worst; rates for Hispanics were intermediate, but well below those for non-Hispanic white women. Breast cancer is increasing rapidly among Hispanic women, with the incidence rate up by 56 percent over the 19 years of available data (1969–1987) and the mortality rate increased by nearly 100 percent over 30 years (1958–1987). Breast cancer SEER data (1988–1990) from California indicate that incidence rates for all ages overall are about 20 percent higher among whites than African Americans; age-adjusted rates per 100,000 for Hispanics and Asian/Other women are about half the rate for whites. Breast cancer mortality is 15 percent higher for African American women in that state than the rate for white women in that state, with rates for Hispanics and Asian/Others about half the breast cancer mortality rate for white women. As most cancer registries do not collect survival data, current survival data is limited and what is available is either too old or not yet analyzed and published.

CLINICAL RESEARCH

These data indicate that reducing the survival disadvantage for minority women, particularly African American women, is most likely to be achieved through strategies aimed at early recognition of disease. NCI supports studies covering all aspects of breast cancer research, including early detection and screening, diagnosis and prognosis, treatment, prevention and control, and outreach and education. We support research that applies to all women; we also support research aimed at minority and underserved women to ensure that we have data appropriate to minorities and that these women get the culturally appropriate cancer information they need to make informed choices about their health care.

To assure our ability to obtain accurate data to formulate cancer control and intervention strategies, NCI has been a leader in developing a wide range of efforts designed to address the increased cancer burden borne by minority populations. The NIH Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research, as required by the NIH Revitalization Act of 1993, require that NIH:

- ensure that women and minorities and their subpopulations are included in all human subject research;
- for Phase III clinical trials, include women and minorities and their subpopulations such that valid analyses of differences in intervention effect can be accomplished;
- not allow cost as an acceptable reason for excluding these groups; and
- initiate programs and support for outreach efforts to recruit and retain these groups as volunteers in clinical studies.

Clinical trials serve as one of the foundation stones of the National Cancer Program. They are the real-world test of which new therapies (or preventive measures) will benefit specific patients. The key components of all clinical trials include careful and scientifically appropriate protocol design, informed consent, data management, quality control, and publication of trial results based on thorough statistical analysis. When all of these components are in place and functioning smoothly, we can have confidence in the results of clinical trials.

The NCI has a history of representative numbers of women included in clinical studies, and has fostered and cultivated relationships with communities of color nationwide to encourage their participation, as well. We support a large national network of Community Clinical Oncology Programs (CCOPs), Clinical Trials Coopera-

tive Groups (Groups), and Cancer Centers that provide state-of-the-art care for patients and perform clinical trials designed to develop better therapies. Today we support 27 Comprehensive Cancer Centers across the country, which have a mandate to bring advances in cancer prevention, detection, and treatment to their communities and to develop strong links with community physicians and support groups. We support 30 other specialized centers and have recently awarded planning and development grants to develop new centers or consortiums that will either be located in geographically underserved areas of the United States or specifically target minorities or other underserved populations. The Groups were established in 1975 and now conduct approximately 35 breast cancer treatment trials that enroll 5,000 new patients each year. The establishment of CCOPs in 1983 created a network of community cancer specialists, primary care physicians, and other health care professionals who conduct clinical research on treatment, cancer prevention and control, screening, chemoprevention, smoking cessation, patient management, continuing care, and rehabilitation. The program involves more than 300 hospitals and nearly 2,500 physicians. We have evaluated the CCOP model and have found that it is an effective mechanism for linking investigators and their institutions with the Groups network; accordingly, Minority-Based CCOPs (MBCCOP) were initiated in 1990 to provide minority cancer patients increased access to state-of-the-art cancer treatment and prevention and control technology. Eight MBCCOPs are now funded, involving more than 25 hospitals and over 200 physicians, and more than 50 percent of their new cancer patients are from minority populations.

You have asked NCI if minority women in our sponsored breast cancer clinical trials are represented in numbers comparable to their numbers in the general population. I can answer most emphatically that African American women are. SEER data indicate that 8.6 percent of women diagnosed with breast cancer in 1991 were African American. For the period 1991–1994, 9.8 percent of women who were randomized to clinical trials in the cooperative group breast cancer studies who chose to report their racial or ethnic category were African American. Minority accrual from the CCOP components of these cooperative groups was included in this figure.

By comparison, Hispanic women may be somewhat under-represented on clinical trials, although this is difficult to evaluate since there are no comparable figures from SEER for the incidence of breast cancer in Hispanic women. However, we can report that some 3.1 percent of the Cooperative Group breast cancer population (which is largely composed of women over age 55) reports itself as Hispanic; 4.5 percent of American women over age 55 are said to be Hispanic.

As our surveillance figures emphasized that different groups had significantly different cancer rates, we increased our research dissemination efforts to specific communities. We are proud that the efforts we began years ago to assure that cancer research could benefit all our nation's citizens are evident in our clinical trials accrual rates. However, minority enrollment to all our trials must still be expanded. Research has shown that obstacles to even greater enrollment of minority women may include poor access to health care associated with lower socioeconomic status; less acceptance by minority women of clinical research participation: lack of insurance, or greater out-of-pocket expenses, to cover non-research costs on clinical trials; fear of being test subjects or "guinea pigs"; lack of information about clinical research; and less willingness by investigators to enroll patients whose follow-up compliance may be perceived as potentially imperfect. Practical factors, such as childcare, transportation, and lost wages may play a role in this problem.

To answer your question, it is very important to provide minorities equal access to research to ensure that results can be generalized to the entire population, particularly if there is no evidence of "differences" based on race, ethnicity, or socioeconomic status. If investigators have reason to believe there may be differences based on these factors, appropriate populations must be included to draw relevant conclusions. There are methods for stratifying subgroups within larger study populations, and this may mean that different, separate studies do not necessarily need to be conducted.

NEW RESEARCH

To address your question about how differences could best be addressed, I would like to take a moment to describe some of the new research findings that may have a significant impact on breast cancer in minority women. Studies at the molecular level are providing information about family patterns and about inherited and acquired gene abnormalities that may influence the development and invasiveness of breast cancer cells. One intriguing door to further research has been opened with the discovery of the BRCA–1 gene (by the University of Utah Medical Center work-

ing closely with the NIH National Institute of Environmental Health Sciences), which is thought to be responsible for about 5 percent of all breast cancers.

It may be important to study whether or not BRCA–1 can explain a portion of the increased incidence in breast cancer that afflicts young African American women. To date, we have not been able to identify any cause or factors related to the higher incidence of breast cancer among African American women under age 45 compared with white women in the same age group. It is possible that the higher incidence among young African American women may be due to a higher percent with genetic predisposition for the disease. It may be possible to develop genetic screening strategies that will enable disease susceptibility to be detected in individuals and thus allow more focused research on possible preventative or early detection methods. With the identification of BRCA–1 on September 14, 1994, work is already underway to identify high risk African American women and possible family structures and analyzing gene structures of those women.

Another provocative discovery is the recent finding of mutations in the p53 tumor suppressor gene in a group of African American women from Michigan. The types of mutations seen suggest the need for further research regarding environmental and occupational factors in cancer development, and may lead to important findings about individual risk assessment and monitoring responses to various cancer prevention interventions.

This research can be greatly facilitated through the new Cooperative Breast Tissue Registry which will make available to scientists large numbers of breast tumor specimens with their associated clinical and outcome data. The Registry is developing a central database that will maintain an inventory of specimens including information about the date of diagnosis, stage, grade, nodal status, brief treatment history, recurrence information, and vital status. Over 20,000 specimens are expected to be included in the initial inventory which will allow comparisons to be made between various subpopulations. Tissue specimens from minorities are represented in the registry and an effort is being made to increase the number of specimens from these groups.

Early detection methods and state-of-the-art therapies clearly can save lives; experts estimate that when a breast tumor is found in the earliest stages, the 5-year survival rate is 96 percent. Unfortunately, while research has proven mammography for women aged 50 and over saves lives, data are uncertain for women in their 40's. We are continuing research on early detection methods, and through workshops and meetings we are encouraging the development of new digital mammography technology and other imaging and detection methods. With the discovery of the genetic components of breast cancer, scientists are working to use these components to increase the precision and sensitivity of diagnosis and the accuracy of prognosis for breast cancer. Blood tests may be able to identify carriers of the genes that may be associated with increased risks.

Another research development is particularly promising. We are learning how to "turn off" certain genes responsible for tumor growth. New research is underway to investigate the reasons for the aggressive growth of breast cancer cells in African American women. In the Li-Fraumeni syndrome, families inherit a predisposition for certain cancer by inheriting mutations in p53 (the tumor suppressor gene), including breast cancer, and we are looking for ways to perhaps control this process. The role of growth factors is also under study, as are experimental approaches to vaccine development.

Environmental factors, such as alcohol, certain medications, hair dye, electromagnetic fields, occupational exposures, and pesticides, are all under study in NCI-funded projects such as the Long Island Breast Cancer Study Project, the Northeast/Mid-Atlantic Study, and the Triana, Alabama study of African Americans exposed to extremely high levels of organochlorines. The Women's Health Initiative, a trans-NIH clinical trial, is testing interventions to prevent cancer, cardiovascular disease, and osteoporosis and is targeting interventions to underserved and minority populations. The NCI Women's Health Trial: Feasibility Study in Minority Populations is testing methods to enable African American, Hispanic, and low income groups to change to low fat diets.

Another study was recently completed of breast cancer in women under age 55 of Asian ethnicities living in San Francisco, Los Angeles, and Hawaii. The study looked at factors such as adolescent and childhood diet, height, weight, and other lifestyle factors, to determine risk of breast cancer over generations, and the higher incidence of cancer for women under age 40. Women under age 45 were also studied in Atlanta, Seattle, and Trenton to address a variety of etiologic hypotheses, including the relationships of risk to diet, body size measures, and contraceptive practices. Results from both of these studies are currently being analyzed.

NCI has also begun a randomized clinical trial in the CCOP network that will study the preventive effect of the antiestrogen tamoxifen on women at high risk for developing breast cancer. The Breast Cancer Prevention Trial (BCPT) is the first large-scale chemoprevention trial ever undertaken to prevent breast cancer from occurring in healthy women. Before the trial was initiated, the investigators were instructed about NIH guidelines and the requirement that minority racial and ethnic groups be represented proportionately. We are pleased that we and other investigators have found creative approaches to ensuring that minorities are accurately represented.

Each clinical center was directed to plan for the recruitment of special populations for its unique situation. Consultants were invited to provide the leadership with accrual strategies; regularly held meetings with investigators continue to seek new approaches to enhancing minority voluntary accrual; a public service announcement geared to women of color is being produced; minority recruitment specialists are working with recruitment sites; and funding has been provided to cover the costs of trial participation for the economically disadvantaged. The NIH Office of Research on Women's Health (ORWH) has added supplemental funds to the BCPT to fund a demonstration/evaluation project to assist BCPT centers in the design of minority recruitment programs (known as SPRT—Special Population Recruitment Team). In the most recent recruitment data, 4 percent of the women entering the trial are minorities. We are pleased to say that risk assessments submitted in August 1994 are the highest ever for African American and other racial groups, at 19 percent of all assessments submitted. If these efforts lead to increased risk assessment and accrual, they will be integrated into the accrual process for other trials.

OUTREACH

NCI alone cannot conquer breast cancer. We need the specialized expertise of other Federal agencies, state health departments, academia, industry, local businesses, consumers, and consumer groups, to move forward with our mission and we appreciate the support that has been given us by Congress. Our nationwide effort to involve local communities in cancer awareness and control projects has been underway for almost two decades. An exciting and important example of our community-based cancer control outreach programs can be found with the Leadership Initiatives, which include the National Black Leadership Initiative (NBLIC), the National Hispanic Leadership Initiative, and the Appalachian Leadership Initiative. Their objectives are to develop community coalitions that will implement effective cancer control intervention programs and strategies, and provide data for collection and research efforts. One of the breast cancer activities undertaken by the NBLIC is the establishment by each NBLIC regional office of a resource directory of health facilities that offer free or low cost mammograms.

Other premier initiatives include:

- Collaboration with Revlon, the National Broadcasting Company, and the National Association of Broadcasters, on developing and distributing a videotape, "Once a Year . . . for a Lifetime," in both English and Spanish.
- NCI's Intramural Clinical Oncology program seeks candidates for protocol entry through a comprehensive mailing of referral letters through the American Medical Association listing of physicians and directs correspondence to rural underserviced districts as well as overpopulated cities with substantial minority populations.
- The National Cancer Control Research Network for Black Americans was established to increase the number of African American cancer research scientists, expand research in cancer among the African American population, and encourage collaboration. Other networks are established for Native Americans, Hispanic Americans, and Native Hawaiian and American Samoans.
- NCI has developed an easy-to-read cookbook of traditional recipes for African Americans called "Down Home Healthy," which is culturally relevant and meets NCI's dietary guidelines. We are also working with the food industry on our groundbreaking "5 A Day For Better Health" dietary campaign.
- NCI awarded contracts to explore approaches to building cancer prevention awareness in the community through historically Black colleges and universities. NCI provides materials and technical assistance to these institutions as they plan and implement outreach strategies.
- NCI participated with the Centers for Disease Control and Prevention and the Food and Drug Administration in developing the Assistant Secretary for Health's National Strategic Plan for the Early Detection and Control of Breast and Cervical Cancers. This should provide impetus to current activities in early detection and followup to ensure every woman receives appropriate screening.

• The NCI's Cancer Information Service toll-free number (1–800–4–CANCER) is a regionally-based service tailored to the communities it serves and provides information about clinical trials and state-of-the-art treatment.
• The NCI develops and distributes publications and conducts national educational campaigns about reducing cancer risk, such as our ASSIST and COMMIT tobacco intervention and control projects.
• We develop fact sheets and press statements to disseminate new and important information to the press and the public as quickly as possible.
• Pamphlets describing What You Need to Know About . . . . various cancers are available, and include all known risk factors and preventive actions regarding the specific cancer. Spanish-language and low-literacy versions of these pamphlets are being developed.
• The NCI and the Susan G. Komen Breast Cancer Foundation are cosponsoring breast cancer education summits around the country to encourage leaders of businesses, community and voluntary organizations, and health organizations, to sponsor or establish breast cancer education and screening activities and programs in their community.
• NCI is testing community telephone counseling and other strategies to increase breast cancer screening in low-income, minority, and underserved populations.
• NCI is supporting activities in Hawaii to reach Native women with information about mammography an early detection, and investigators are researching ways to make available materials more culturally appropriate.
• NCI worked with a panel of ethnic population advisors to develop low-literacy nutrition education materials for African Americans, Hispanics, Asian Americans, Native Hawaiians, Alaska Natives, American Indians, and the rural underserved. These are now available on early detection of breast cancer and other cancers.
• We are funding a national survey to monitor mammography facilities to provide a representative profile of practices based on regional variation.
• NCI, in collaboration with the National Institute of Environmental Health Sciences, ORWH, and the National Institute for Occupational Safety and Health, sponsored an international conference on occupational cancer among women, including minority women. The meeting emphasized clarifying the methodologic problems and suggesting ways to overcome research and assessment obstacles, identifying data resources, defining research needs, and stimulating further research.

CONCLUSION

Through its extramural and intramural programs, NCI supports intensive, integrated investigations in prevention, early detection, treatment and quality of life. It is fitting that the full spectrum of integration of basic science and clinical innovation, from molecular genetics to molecular medicine, is most clearly developed for breast cancer, the most common cancer in American women. Our knowledge about breast cancer is increasing, yielding steadily to the insights gained through basic and clinical investigation. There are realistic prospects for major progress toward prevention and cure, but these will require a persistent research effort over many years. These strategies will not succeed unless we reach all our citizens with culturally appropriate messages about fighting cancer. NCI is determined to do that. We must have the help of our citizens to win this war.

I would be happy to answer any questions.

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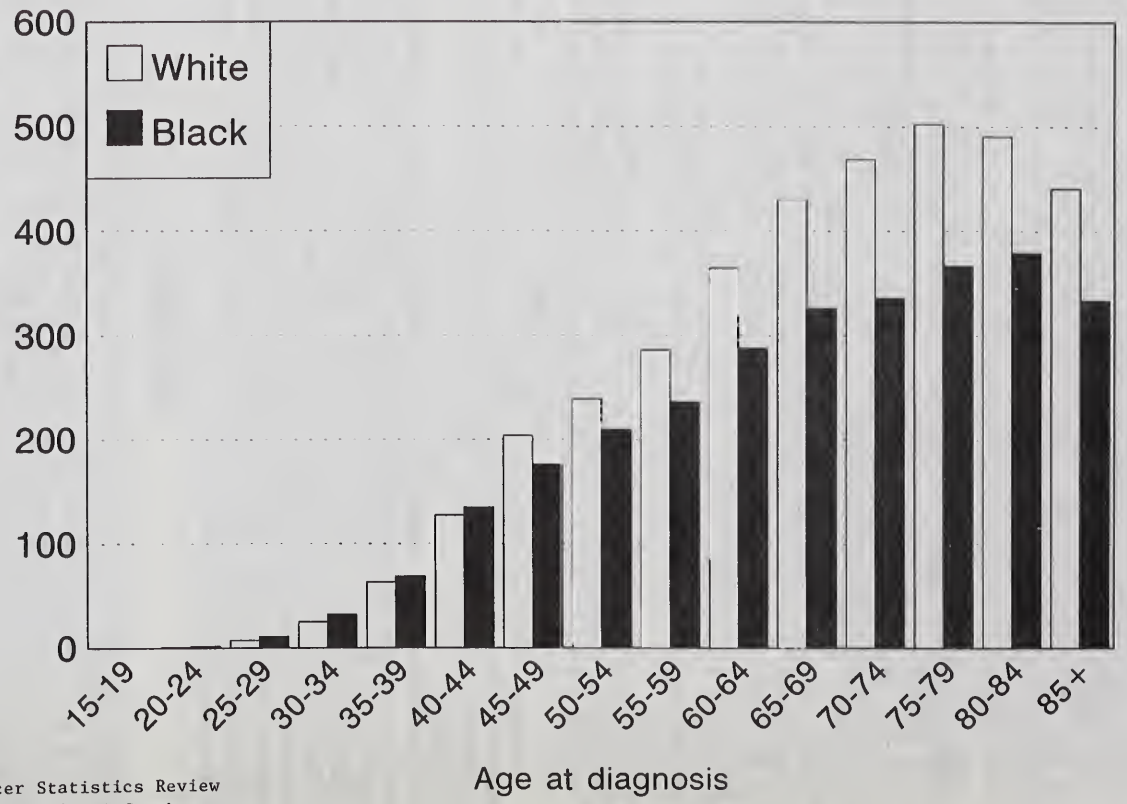
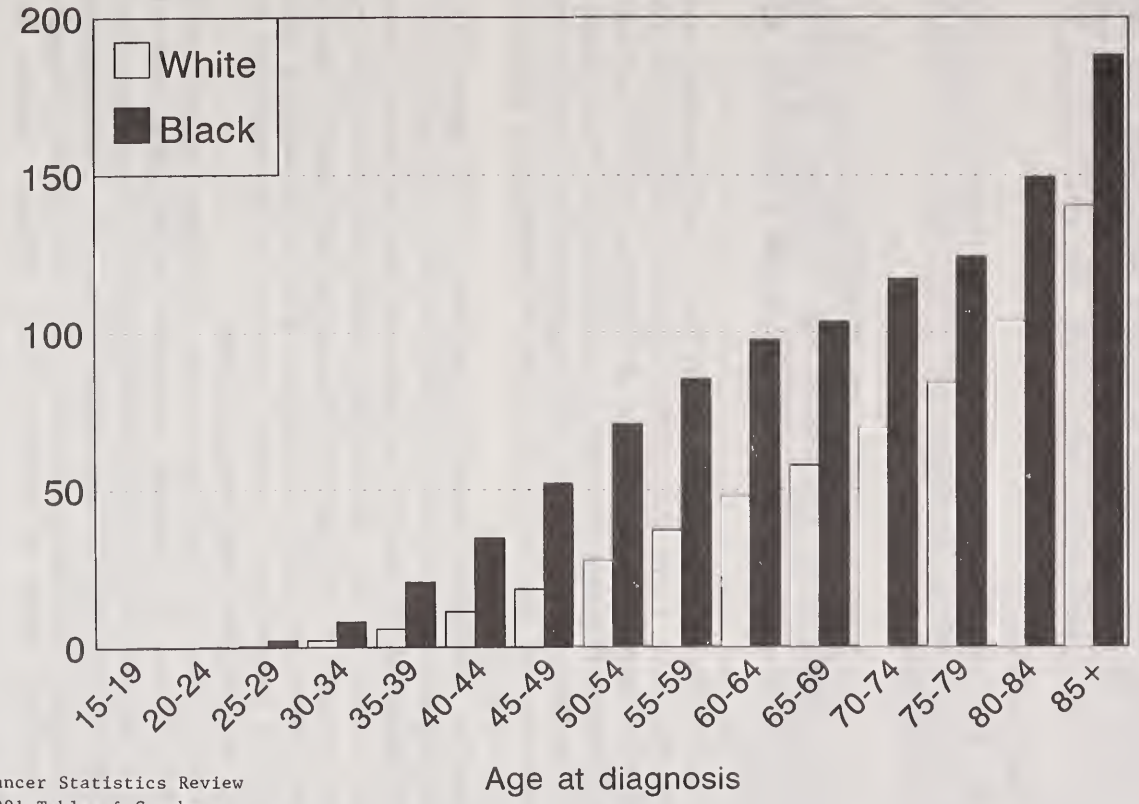
Cases of Breast Cancer per 100,000
SEER, Female, 1987-91



SEER Cancer Statistics Review
1973-1991, Tables & Graphs
NCI Surveillance Program

Breast Cancer Deaths per 100,000
United States, Female, 1987-91



SEER Cancer Statistics Review
1973-1991 Tables & Graphs
NCI Surveillance Program

Mr. TOWNS. Thank you very much.

The noise you heard is the bells indicating that there is a vote on the floor. I would like to ask for a 15-minute break and we will go and vote and come right back. We will have a 15-machine recess.

[Recess taken.]

Mr. TOWNS. The recess went a little longer because there was not one but two votes. So thank you very much, Dr. Sondik.

Ms. Henson.

STATEMENT OF ROSEMARIE M. HENSON, M.S.S.W., M.P.H., ACTING DIRECTOR, DIVISION OF CANCER PREVENTION AND CONTROL, CENTERS FOR DISEASE CONTROL AND PREVENTION

Ms. HENSON. Good afternoon, Mr. Chairman and members of the subcommittee. I am Rosemarie Henson, Acting Director of the Division of Cancer Prevention and Control, with the National Center for Chronic Disease Prevention and Health Promotion, at CDC.

I am pleased to have this opportunity to address the issue of breast cancer and minority women, especially during Breast Cancer Awareness Month.

As the Nation's prevention agency, CDC draws from advances made by our colleagues at NCI in basic research, and applies that knowledge at State and community levels throughout the country. Basic research has shown that early detection of breast and cervical cancers is a major defense against death from these cancers. Using these scientific findings as a springboard for action, the CDC national breast and cervical cancer early detection program supports widespread screening efforts.

Almost one-half million women are expected to lose their lives to breast cancer this decade, despite the fact that more than 30 percent of these deaths from breast cancer in women over 50 are preventable through the widespread use of screening mammography. Breast cancer is the most commonly diagnosed cancers and the second-leading cause of cancer death among women in the United States.

In 1991, over 3,000 women died from breast cancer. Mortality rates for African-American women were disproportionately high. The death rate for African-American women was 19 percent higher than the rate for white women.

We know that the widespread use of screening mammography can save lives. Unfortunately, women are not receiving these lifesaving services. CDC data indicate that only 51 percent of all women age 50 and older had received a mammogram during the preceding 2 years. Only 48 percent of African-American women and 47 percent of Hispanic women age 50 and older reported receiving a mammogram during the 2 previous years.

Congress recognized the importance of creating a national early detection program for all women when it enacted the Breast and Cervical Cancer Mortality Prevention Act of 1990. This landmark legislation authorized CDC to establish a national public health infrastructure to implement State-based breast and cervical cancer early detection programs.

Concurrently, CDC, in partnership with the National Cancer Institute and other Public Health Service agencies, led a private and public sector effort to develop a national strategic plan for the early detection and control of breast and cervical cancers. This plan identifies steps to control these cancers and serves as an important tool in guiding program delivery.

The primary focus is on early detection and follow-up. Aggressive efforts are needed to screen, follow up, and provide treatment for women who are underserved, particularly minority women and women who lack financial resources.

CDC's national breast and cervical cancer early detection system utilizes the plan and supports efforts to increase participation in screening programs among all women, particularly minorities, older women, Native Americans and women of low income. Culturally sensitive strategies to reach minorities and other underserved women received the highest priority.

The fiscal year 1994 appropriation of $78 million enabled CDC to assure greater access to mammography screening and followup service, expand educational programs for women, increase training programs for health care providers and improve quality assurance measures.

Currently CDC supports breast and cervical mortality prevents efforts in 50 States; 26 States are funded to carry out comprehensive programs. Twenty-four States receive funds for planning activities to eventually carry out a comprehensive program.

We are pleased to report that with the fiscal year 1995 appropriation of $100 million, CDC will provide screening services to an additional 8 to 10 States.

As a result of this national program, by March 31, 1994, over 100,000 eligible women received mammography screening in 13 States. Of the total number of women screened, 26 percent were Hispanic, 17 percent were African-American, 11 percent were Native American, and 2 percent were Asian American. Fifty-six percent of all mammography screenings were received by minority women.

We will only be successful in helping women with screening services through intensive community efforts. I would like to highlight a few examples of innovative interventions.

The Witness Program is a breast cancer education program in rural Arkansas targeting African-American women, and supported by the Susan G. Komen Foundation and the Arkansas Cancer Research Center. Programs are presented to small groups of women, usually in local churches. Role models tell personal stories about breast cancer called "witnessing" with a focus on the importance of screening.

In Abilene, TX, the YWCA uses an approach to provide screening services. The YWCA recruits white, Hispanic and African-American women in this predominantly rural area through YWCA churches, clinics, and senior centers. YWCA staff refer women to health care providers for mammograms and pap tests. To increase access to screening they provide a van which transports women to and from screening sites. Support services are provided to women who are diagnosed with breast cancer.

In your State, Mr. Chairman, the State health department has used focus groups to determine the appeal and accessibility of educational materials for uninsured women, Native Americans, African Americans and Hispanic women, as well as migrant workers and rural women. A particular effort was made to identify psychological barriers to comprehensive breast health care.

Another important weapon against breast cancer is public and private partnerships with organizations and groups who share our mission. CDC works closely with many national organizations. For example, the American Cancer Society works with state health agencies to develop innovative education strategies to increase access to screening services for minority and underserved women.

CDC entered into a collaborative agreement with the YWCA of the U.S.A. in 1993 and program activities have been initiated in 30 States. The YWCA has expanded its encore program by adding an early detection component with a grant of $4 million provided by Avon. This comprehensive program includes breast health education, recruitment, outreach, navigation through the screening process, and support services for women with breast cancer.

This year, CDC expanded its partnership with organizations that have access to special populations. Included are the American Association of Retired Persons, the National Caucus and Center on Black Age, the National Hispanic Council on Aging, the Susan G. Komen Foundation and the National Migrant Health Program. The others are listed in the written testimony.

CDC works closely with professional organizations such as the National Medical Association and the American Nurses Association to increase the skills of health care providers to educate African-American women on the benefits of screening mammography.

Through the National Breast and Cervical Cancer Early Detection System, CDC will continue to support the design and implementation of innovative program strategies to increase access to screening and followup services for minorities, older women, Native Americans, and to assure the quality of screening services for all American women.

Thank you for this opportunity to discuss the CDC's breast and cervical cancer prevention efforts. I will be happy to answer any further questions.

[The prepared statement of Ms. Henson follows:]

PREPARED STATEMENT OF ROSEMARIE M. HENSON, M.S.S.W., M.P.H., ACTING DIRECTOR, DIVISION OF CANCER PREVENTION AND CONTROL, CENTERS FOR DISEASE CONTROL AND PREVENTION

Good afternoon, Mr. Chairman and members of the Subcommittee. I am Rosemarie Henson, Acting Director of the Division of Cancer Prevention and Control, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention. I am pleased to have this opportunity to address the issue of breast cancer and minority women, especially during "Breast Cancer Awareness Month." CDC is one of 17 organizations that serve on the Board of Sponsors for the National Breast Cancer Awareness Month Program. Now in its tenth year, this program is designed to increase public awareness of breast cancer. Other sponsors include the National Cancer Institute, American Academy of Family Physicians, American Cancer Society, and the National Medical Association.

As the Nation's Prevention Agency, CDC draws from advances made in basic, behavioral and epidemiologic research, and applies that knowledge at State and community levels throughout the country. Research has shown that early detection of breast and cervical cancers is a major defense against death from these cancers.

Using this scientific finding as a springboard for action, CDC's National Breast and Cervical Cancer Early Detection Program supports widespread screening efforts.

Almost one-half million women (460,000) are expected to lose their lives to breast cancer this decade, despite the fact that more than 30 percent of deaths from breast cancer in women over 50 are preventable through the widespread use of screening mammography. Breast cancer is the most commonly diagnosed cancer and the second leading cause of cancer death among women in the United States. Lung cancer is the leading cause of cancer death among all women. Colorectal cancer is the third leading cause of cancer death.

In 1991, 43,583 women died from breast cancer. Based on CDC's National Center for Health Statistics mortality data from 1991, the death rate for African-American women was 31.9 (per 100,000 women), 19 percent higher than the rate for white women (26.8 per 100,000 women). Rates for black women and white women were 2.6 and 2.2 times higher, respectively, than women of other races.

We know that the widespread use of screening mammography can save lives. Unfortunately women are not receiving these lifesaving services. CDC data indicate that in 1992 only 66% of all women aged 40 and older reported ever receiving a mammogram. Only 62 of African-American women and 666 of Hispanic women aged 40 and over reported ever receiving a mammogram. Only 516 of all women aged 50 and older had received a mammogram during the preceding 2 years. Only 48% of African-American women and 476 of Hispanic women aged 50 and older reported receiving a mammogram during the preceding 2 years.

Programs to reduce breast cancer mortality must emphasize the role of routine mammography screening to detect breast cancer at earlier, more treatable stages. Significant economic, geographic, cultural, and knowledge barriers prevent many women, especially women of low-income (where mortality rates are disproportionately high) from taking advantage of these life-saving technologies.

Congress recognized the importance of creating a national early detection breast and cervical cancer program for all women when it enacted the Breast and Cervical Cancer Mortality Prevention Act of 1990. This land-mark legislation authorized CDC to establish a national public health infrastructure to implement state-based breast and cervical cancer early detection programs.

Concurrently, CDC, in partnership with the National Institutes of Health and other Public Health Service agencies, led a public/private sector effort, to develop a National Strategic Plan for the Early Detection and Control of Breast and Cervical Cancers. This Plan identifies steps to control these cancers and serves as a cornerstone in guiding program delivery. The primary focus is on early detection and follow-up. Aggressive efforts are needed to screen, follow-up, and provide treatment for women who are underserved, including minority women and women who lack financial resources. Implementation of the recommendations will help to achieve specific Healthy People 2000 objectives to increase screening rates among minority women and other underserved women.

CDC's National Breast and Cervical Cancer Early Detection Program is based on the National Strategic Plan for the Early Detection and Control of Breast and Cervical Cancers. The purpose of the Program is to increase participation in screening programs among all women, particularly minorities, the elderly, Native Americans, and women of low-income. Efforts to reach minority and other underserved women receive the highest priority. In addition, CDC worked with the National Cancer Institute and the PHS Office on Women's Health to develop the Secretary's National Action Plan on Breast Cancer, which includes strategies to address all aspects of breast cancer—from prevention to recovery, including early detection.

The Fiscal Year 1994 appropriation of $78 million has enabled CDC to assure greater access to mammography screening and follow-up services, expand education programs for women, increase training programs for health care providers, and improve quality assurance measures for screening mammography (and Pap testing). Currently, CDC supports breast and cervical cancer mortality prevention programs in 50 States and 4 territories: 26 States are funded to carry out full-scale (comprehensive) screening programs with awards ranging from $700,000 to $5 million; 28 States, with awards averaging $300,000 each, receive funds to begin start-up activities to eventually carry-out comprehensive programs. We are pleased to report that with the FY 1995 appropriation of $100 million, CDC will fund an additional 8–10 comprehensive States.

As a result of CDC's National Program, by March 31, 1994, in 13 States, 112,604 eligible women received mammography screening. Of the total number of women screened, 266 were Hispanic, 17% were African-American, 11% were Native American, and 2% were Asian American. Fifty percent of all mammography screenings under this program were received by minority women.

We will only be successful in reaching women with these lifesaving services through intensive community-based efforts. I'd like to highlight a few examples of CDC grant-funded programs that communities and States are employing:

- The Witness Project is a health program aimed at African-American women in churches and community centers across Arkansas. Supported by various organizations, including the Susan G. Komen Breast Cancer Foundation and the Arkansas Cancer Research Center, the project develops community-level breast cancer education programs; provides continuing medical education to local physicians, nurses, and technologists to improve diagnostic techniques and appropriate referral of symptomatic breast cancer patients; and evaluates the influence of breast cancer education and services interventions.
- In California, an effective approach to reach Hispanic women has been developed by a consortium of community-based organizations. The "comadre," or community gatekeepers, inform, educate, and recruit into screening women who are unfamiliar with the health care system. This approach brings the program to women in need by establishing outreach sites in housing units and local churches.
- In Abilene, Texas, the YWCA uses an innovative approach to providing screening services through "brokering". The YWCA recruits white, Hispanic, and African-American women in this predominantly rural area through YWCA programs, churches, clinics and other locations. YWCA staff refer women to health care providers for the mammograms and Pap tests. To increase access to services, the YWCA provides a van which picks up women who need transportation and takes them to and from the screening sites. The YWCA ensures that women with abnormal tests receive the follow-up services they need, and provides resources to pay for follow-up services for women who cannot afford them.
- In New Mexico, community outreach to African-American women is facilitated though training of low-income community women and guided by a committee of community leaders, the African-American Breast and Cervical Cancer Prevention Committee.
- In Nebraska, a seminar on breast and cervical cancer, developed by and for women in the community, was jointly sponsored by the Omaha Black Nurses Association, the Nebraska Department of Health, the Delta Sigma Theta Sorority, and the American Cancer Society. One young woman who attended the seminar had a palpable lump and had been unsuccessful in gaining access to the health care system. This outreach program provided her with the support and services she required.
- The State of New York has used focus groups to determine the appeal and accessibility of educational materials to the uninsured and underinsured, women of low-income, Native American, African-American, and Hispanic women, as well as migrant workers and rural women. Particular effort was made to discover psychological barriers to comprehensive breast health care. New York is also initiating several surveys of Hispanic, African-American, Native American women and migrant workers to determine their attitudes and behaviors regarding cancer screening. These surveys will enable the program to identify specific gaps, barriers and risk factors that limit access to and utilization of comprehensive early detection.
- This year, CDC began a major initiative to directly fund eight Indian tribes and tribal organizations to establish comprehensive early detection programs for American Indian women. CDC has assigned a staff person to work with the Indian Health Service to help States reach Native American women.

It is important to note that payment for preventive health services (like mammography and Pap testing) is futile without comprehensive, consumer directed "recruitment systems" to ensure widespread participation. In other words, it isn't enough to just pay for the services—we must develop ways to reach women who have previously not had access to services.

Another important weapon against breast cancer is public/private partnerships—cooperative alliances with organizations and groups who share the same mission. Let me share with you some examples of the efforts of these partnerships to enhance State and community-based activities:

- The Young Women's Christian Association (YWCA) has made available to 30 States its resources, programs, and expertise in health promotion, including the capacity to provide ancillary services such as transportation, day-care, counseling, education, and peer support; and its ability to offer critical follow-up for women diagnosed with breast cancer. Its Encore and Encore-Plus programs educate African-American women about breast health and provide support for women with breast cancer. In addition, Avon Products Incorporated formed a

partnership with YWCA. Through the sale of breast cancer screening awareness pins, Avon raised $4 million dollars for education and outreach programs.

• The American Cancer Society's many volunteers and staff are working together with State agencies to develop innovative strategies in educational outreach and health promotion for hard-to-reach populations.

This year, CDC expanded its partnerships with organizations that have access to populations of special interest—Native Americans, African-Americans, Hispanics, older Americans, the homeless, and low-literacy audiences. These new partners include: the American Association of Retired Persons, American Federation of Teachers Education Foundation, American Indian Health Association, Coalition of Hispanic Health and Human Services Organizations, Mayo Foundation Inc., National Caucus and Center on Black Aged Inc., National Education Association, National Hispanic Council on Aging, National Migrant Health Program, Susan G. Romen Breast Cancer Foundation, and World Education.

CDC works in partnerships with professional organizations such as the National Medical Association and the American Nurses Association to increase the skills of health care providers to educate African-American women on the benefits of screening mammography.

Through the National Breast and Cervical Cancer Early Detection Program, CDC will continue to support the design and implementation of innovative program strategies to increase access to screening and follow-up services for older women, minorities, American Indians, and women of low-income, and to assure the quality of screening services for all American women.

Thank you for this opportunity to discuss CDC's breast and cervical cancer prevention activities. I will be happy to answer questions.

Mr. TOWNS. Let me thank you for your testimony.

It never fails. Believe it or not, we have another vote. This time I will try to make it a 10-minute recess and hope we will be able to be back by that time. It never fails.

[Recess taken.]

Mr. TOWNS. I apologize again. It has been just awful, I tell you.

Let me begin by first saying, regarding the black-white cancer survival study, which was published I think last week——

Ms. MORGAN. You still have one more piece of testimony on the panel, don't you? Dr. Edwards.

Mr. TOWNS. No, I have covered the panel.

Am I correct in understanding that whether women had insurance or not was a major factor in their survival rate?

Dr. SONDIK. Let me ask Dr. Edwards to answer that question, the author of the study.

Dr. EDWARDS. Yes, in our study we looked at many factors, including the usual source of health care and health insurance, and these were factors that could predict outcome.

Mr. TOWNS. Is it true that lack of insurance was more important even than poverty levels or educational levels except that poor women might be less likely to have insurance?

Dr. EDWARDS. I don't believe we came to that conclusion when we looked at all the factors at the same time. I will stop there.

Mr. TOWNS. Did the importance of insurance extend across the two groups? Was it true that both black and white women were more likely to die from breast cancer if they lacked insurance?

Dr. EDWARDS. I believe the survival or risk ratios were worse among those that had no insurance, yes, for both black and white women, compared to the risk ratios for the poverty index.

Mr. TOWNS. Ms. Henson, let me just say I am encouraged by the CDC's response to the congressional mandate and by your efforts to reach minority women. I note the number of women screened in your testimony, given that one of the goals is regular screening,

what has this plan done to improve regular mammography screening?

Ms. HENSON. The resources that are provided through the Breast and Cervical Cancer Mortality Act have enabled States and communities to target underserved women. We have been able to reach a higher proportion of African-American women, Hispanic women, Asian women, and American Indian women.

So previous to this act we didn't have resources to do early detection. Now we have comprehensive programs funded in 26 States across the country.

Mr. TOWNS. Let me say, and I want to say this first, I applaud you for your work so far. But is it safe to say that CDC still has a long way to go?

Ms. HENSON. Yes.

Mr. TOWNS. To reach, say, even half the minority women in this country?

Ms. HENSON. Yes. That is an important question. We need to have much better data in terms of what that denominator is. We know, for example, let's take the State of New Mexico. We put $3.2 million in New Mexico. We know we are meeting 38 percent of the need of the women that would be eligible for this program.

In your State, in New York State, we provide New York State with $3.7 million. New York is very fortunate that they have State appropriations for screening as well. But we know that we are only going to meet 2 to 3 percent of the need there. There are a lot of women that don't have access to early detection services in this country.

Mr. TOWNS. The clear message I am getting is that early detection is crucial to survival. Can I take it that all of you agree on that? Starting with Dr. Christian, all the way cross?

Dr. EDWARDS. Yes.

Dr. SONDIK. Yes, very much.

Mr. TOWNS. Everybody agrees on that.

At younger ages especially, our tools are not as effective as they are for older women. What is NCI doing to develop more accurate screening techniques, either through improved mammography or through new techniques?

Dr. SONDIK. Thank you, Mr. Chairman. I would be happy to answer that.

We are doing I think quite a bit. First of all, we are analyzing the existing trials on mammography—or we intend to do this if it is approved by one of our boards over the coming weeks—to see if in fact we may be able to determine just how effective mammography is for specific age groups, for example, women 45 to 49. To date, in combining the trials, we have not been able to see results over a narrow age range.

We are working with English investigators on a clinical trial to help support that trial, which we think may be able to help answer the question as to how effective mammography is. But in terms of new techniques, there is a great deal going on, from research on digital mammography to research on MRI, on PET, and on enhancing existing conventional mammography through digital techniques.

All of that research is under way. In fact, on October 11, we are going to be having a briefing under the aegis of NCI and the DHHS Office of Research on Women's Health, Dr. Susan Blumenthal's office, that will be concerned with showing how technologies outside of the traditional area, technologies that have been used in the military and in NASA, could potentially be applied to the breast cancer problem. And we already have research under way in that area.

We are doing what I hope is a great deal toward trying to improve imaging. At the same time we are conducting research on biomarkers that may enable to us find the cancer early and then be able to intervene.

Mr. TOWNS. Will this also help early detection in younger women?

Dr. SONDIK. There is no question about that. The evaluation will be done in women of all ages. The main problem we have, of course, is detecting cancer in younger women.

Mr. TOWNS. We discussed the results of the black-white study, which are certainly important in our policy decisions. Does NCI have similar information on Hispanic women or Native American women? If not, when will such information be available?

Dr. SONDIK. From the statistics that are collected from the SEER program, we have certain indications of information related to the black-white study, but we certainly have nothing in great depth there.

For example, Native Americans have the worst survival from breast cancer of any group in the country. That low survival clearly has to do with access to quality care and appropriate detection.

And I think that cancer control interventions, either through NCI, or through CDC, could improve their prognosis.

In terms of when we will have more precise information, I am sorry to say that it is going to be some time. This information I believe, will be derived from the kinds of surveillance efforts that are now under way. For example, we are building pilot registries that are collecting data on mammography. One of these registries is in the San Francisco area, and it has already provided very valuable information concerning the sensitivity of mammography.

This type of information on minority populations we probably can have in several years. But the kind of black-white study that we just finished is something that would take many, many years, perhaps—certainly well over a decade. The current study, as Dr. Edwards can attest to, took over a decade to complete.

Mr. TOWNS. Well, let me thank all of you again for your testimony. And I apologize, I think everything that could go wrong has gone wrong.

There is a markup that is going on, too, at the same time now, which was scheduled to start at 4:15. A lot of the members of the committee are now at the markup. The markup is on unfunded Federal mandates, so you can imagine that there is a lot of interest in that as well.

Let me thank all of you for your testimony. We look forward to working with you, and I hope we will be able to get more minority patients into the trial. I think that is very, very important, because there seems to be a real problem in this area.

So, Dr. Sondik, in particular, we look forward to working with you to see if we can't do something about this issue. And, as it is National Cancer Awareness Month, I think it is appropriate that we have this hearing at this time. We thank all of you for your testimony.

Our second panel is Dr. Siegel of the Cancer Center of George Washington University, and Dr. Richard Elledge of the University of Texas Health Science Center at San Antonio.

Let me thank you for coming, and here again, I apologize for holding you, but it has been something that I could not control. These votes have just been going on and on. In fact, there is one going on now.

So why don't you begin your testimony. We will try to get through the testimony before I go and vote. Why don't we start with you, Dr. Siegel.

STATEMENT OF ROBERT S. SIEGEL, M.D., INTERIM MEDICAL DIRECTOR, CANCER CENTER, GEORGE WASHINGTON UNIVERSITY MEDICAL CENTER

Dr. SIEGEL. I will try to talk quickly.

Mr. TOWNS. Thank you.

Dr. SIEGEL. I appreciate your invitation to address this subcommittee regarding the important issue of minority women and breast cancer.

My interest in this issue arose several years ago when, during the preparation of our cancer program's annual report, we found that the incidence of breast cancer among young black females was very much increased over the rate found among white females at our institution.

Past studies have documented the death rate among black patients with breast cancer was increased compared to white patients and that black patients were consistently diagnosed at more advanced stages. A clear explanation for these findings, however, has never been identified.

Various factors have been postulated to explain the survival differences, including decreased access to screening, decreased educational levels and less aggressive treatment.

The report that was published in last week's JAMA has been discussed. The conclusion that is important is that the best opportunity in 1994 and for the foreseeable future for reducing the survival disadvantage for black women is to improve strategies for early recognition of breast cancer, facilitate access to primary care and mammography, and increase compliance with current screening recommendations.

Our study utilized information that was derived from all patients who were diagnosed with breast cancer between January 1, 1987, and December 31, 1993, at our medical center. A total of 445 white women and 253 black women with stages 1 and 2 breast cancer were studied using our medical center's cancer registry.

The cancers within the two stages were compared for their pathologic features, treatment, stage of cancer when presenting for medical attention, and survival. The information we have available clearly reveals that the overall survival for all black patients and

for those with stage 2 disease were significantly worse when compared to white women.

In addition, black patients were significantly more likely to be stage 2 at diagnosis compared to white women and were also found to have pathologic characteristics that suggested more aggressive disease.

In the poster that I have on the easel here, just to go quickly, the last two lines I think are the most important, which is, if you look at the black squares representing white women and then the line below that represents the significantly diminished survival of African-American women at 7 years after diagnosis, remembering that we are comparing stage 2 patients to stage 2 patients with equal access to treatment and we have documented in the study that we have done that treatment was the same.

I believe that the explanation for diminished survival among black patients is the more aggressive biologic behavior of their breast cancer, a finding which was clearly demonstrated in our study. For example, black women were significantly less likely to have breast tumors which are estrogen-receptor positive, a characteristic that is associated with a slower growing cancer but also a feature which precludes the use of anti-estrogen hormones, an important component treating both early and advanced cancer.

Other features such as the growth rate of the breast cancer and the degree to which the breast cancer cells resembled normal breast tissue were also found to be less favorable among black patients.

The explanation for the more aggressive biologic behavior of breast cancers seen in black women is unknown. Possible explanations include differences in genetic susceptibility or environmental factors.

Although conducted completely independently, our investigation demonstrates essentially the same conclusions as the study published in last week's Journal of the American Medical Association.

And I am just going to skip here. The information derived from these studies I believe should be utilized in two ways involving both clinical service and research. And I think at this point it is important to point out that the therapy of breast cancer has not changed substantially in 20 years. And that is the reason why the most important way that an individual can improve her chance for cure remains early detection.

In terms of clinical service, the kinds of resources which a government or any institution could help provide include, No. 1, there is an enormous need in the black underserved community for improved access to breast cancer screening, including mammography. Unfortunately, these needs go beyond simple access to insurance. The hardships which women in areas such as Anacostia in the District of Columbia must endure in order to obtain mammography are discouraging, to say the least with more aggressive biologic behavior, the need for more aggressive screening is amplified.

The underserved black community would also greatly benefit from an improved education program. Only as women develop an awareness of the need for early detection of breast cancer, cervical cancer, and other cancers can they be active participants in their own care.

Third, cancer screening, by definition, must occur on a serial basis. I believe women must be incorporated and integrated into a reliable and responsive primary care situation in order to benefit from clinical services and screening techniques.

And finally, there is a need to educate and reeducate primary care practitioners in all communities including the underserved, predominantly African-American areas. Several studies as well as my own experience have documented the absence of a clear understanding on the part of the primary practitioners of the latest guidelines for screening for all types of cancers, including breast cancer.

And then, finally, the explanation for the more aggressive biologic behavior of breast cancers found in black patients is either a consequence of genetic factors or environmental factors. As research priorities are developed for future funding, additional attention should be focused on the need to understand why the differences in biologic behavior exist.

The genetic basis for 10 to 15 percent of cancers has been uncovered recently. Additional genetic defects causing increased susceptibility have yet to be identified.

Further work is clearly necessary. Diet, for example, is an additional variable that merits further work. Answers to these questions will be beneficial not only to the black population but to all women who continue to live in fear of this dreaded disease.

Finally, if I may make one additional statement, and that is that with the CDC discussion and the NCI funding discussion, I want to point out that Washington, DC has unique problems with regard to screening resources. Until this summer, the DC government was given funding which in turn was given to the District of Columbia Cancer Consortium which administered the breast and cervical screening program in the city.

Earlier this summer, the DC government cutoff all funding to the cancer consortium and consequently the screening efforts were halted. One of the things we are working toward at our institution is trying to reinstitute screening, particularly in the underserved parts of this city.

Thank you for listening.

[The prepared statement of Dr. Siegel follows:]

PREPARED STATEMENT OF ROBERT S. SIEGEL, M.D., INTERIM MEDICAL DIRECTOR, CANCER CENTER, GEORGE WASHINGTON UNIVERSITY MEDICAL CENTER

I appreciate your invitation to address this subcommittee regarding the issue of minority women and breast cancer. My interest in this issue arose two years ago when, during the preparation of our cancer program's annual report, we discovered that the incidence of breast cancer among young black females was increased above the rate found among young white females at our institution.

Past published studies have documented that the death rate among black patients with breast cancer was diminished compared to white patients and that black patients were consistently diagnosed at more advanced stages. A clear explanation for these findings, however, has never been clearly identified.

Various factors had been postulated to explain the survival differences including decreased access to screening, decreased educational levels and less aggressive treatment. A report published in the September 28, 1994, issue of the Journal of the American Medical Association presented the results of the National Cancer Institute's black/white cancer survival study (WBCSS). The study revealed that black patients had a two-fold greater increased risk of dying from breast cancer during the study period. Approximately 40% of the difference in survival was explained by more advanced stage of disease at diagnosis among black women. Another 15% of

the survival difference was explained by the fact that white women had less aggressive breast cancers as assessed by their microscopic features. Importantly, lack of health insurance was also a strong predictor of early death. Women without health insurance had two to three-fold increased risk of dying from breast cancer compared to those with health insurance. Differences in treatment could not explain the magnitude of the survival differences. The conclusion of the study was that the best opportunity for reducing the survival disadvantage for black women is to improve strategies for early recognition of breast cancer, facilitate access to primary care and mammography, and increase compliance with current screening recommendations.

Our study utilized information derived from all patients who were diagnosed with breast cancer between January 1, 1987 and December 31, 1993 at our medical center. A total of 445 white women and 253 black women with stages I and II breast cancer were studied using our medical center's cancer registry.

The cancers within the two stages were compared for their pathologic features, treatment, stage of cancer when presenting for medical attention, and survival. The information we have available clearly reveals that the overall survival for all black patients and for those with stage II disease were significantly worse when compared to white women.

In addition, black patients were significantly more likely to be stage II at diagnosis compared to white women and were also found to have pathologic characteristics that suggested more aggressive disease.

I believe that the explanation for diminished survival among black patients is the more aggressive biologic behavior of their breast cancer, a finding which was clearly demonstrated in our study. For example, black women were significantly less likely to have breast tumors which are "estrogen receptor positive", a characteristic that is associated with a slower growing cancer but also a feature which precludes the use of anti-estrogen hormones, an important component in treating both early and advanced cancer. Other features such as the growth rate of the breast cancer and the degree to which the breast cancer cells resembled normal breast tissue were also found to be less favorable among black patients.

The explanation for the more aggressive biologic behavior of breast cancers seen in black women is unknown at this time. Possible explanations include either differences in genetic factors or in environment.

Although conducted completely independently, our investigation demonstrates essentially the same conclusions as the study published in last week's Journal of the American Medical Association. Specifically, both studies document that survival among black patients with the same stage of disease is diminished when compared to white patients, even if treatment is the same. Our study was unique in that each breast tumor was reviewed by a single group of pathologists. Our patients had similar access to care and received the same treatments.

Information derived from these studies should be utilized in two ways involving clinical service and research.

CLINICAL SERVICE

Even without suffering from more aggressive breast cancers, there is an enormous need in the black, underserved community for improved access to breast cancer screening including mammography. Unfortunately, these needs go beyond simple access to insurance. The hardships which women in areas such as Anacostia must endure in order to obtain mammography are discouraging. With more aggressive biologic behavior, the need for screening is amplified.

The underserved black community would also greatly benefit from improved education. Only as women develop an awareness of the need for early detection of breast cancer, cervical cancer, and other cancers can they be active participants in their own care.

Thirdly, cancer screening, by definition, must occur on a serial basis. Women must be integrated into a reliable and responsive primary care situation in order to benefit from clinical services and screening techniques.

Finally, there is a need to educate and re-educate primary care practitioners in all communities including underserved, predominantly African American areas. Several studies as well as my own experience have documented the absence of a clear understanding on the part of primary practitioners of the latest guidelines for screening for all types of cancers.

RESEARCH

The explanation for the more aggressive biologic behavior of breast cancers found in black patients is either a consequence of genetic factors or environmental factors such as toxins in the water or dietary factors. As research prior-

ities are developed for the near future, additional attention should be focused on the need to understand why the differences in biologic behavior exist.

Answers to these research questions will be beneficial not only to the black population but to all women who continue to live in fear of this dreaded disease.

Thank you for your attention.

Mr. TOWNS. I thank you very much for your testimony.

Dr. Elledge, I would like to try to get you in. What I will do is that after your testimony, I will hold the record open for 10 days and we will submit questions. I don't want to hold you any longer, because there is a markup going on, and of course these votes, I don't know how long they are going to go on. So why don't we try and get you in before I run to vote.

STATEMENT OF RICHARD M. ELLEDGE, M.D., DIVISION OF ONCOLOGY, UNIVERSITY OF TEXAS HEALTH SCIENCE CENTER

Dr. ELLEDGE. I am from the University of Texas at San Antonio. Our specialty over the past 15 or 20 years has been tumor biologic factors in breast cancer, sometimes called prognostic factors. We recently completed a very large study looking at tumor biologic factors in Hispanic and black women.

The overall incidence of breast cancer is lower in blacks and Hispanics compared with whites. A closer analysis shows this lower incidence is seen primarily in older women, differences gradually narrow with decreasing age, until around age 40 or 45 the incidence is approximately equal. In younger women, those less than 35, breast cancer may actually occur slightly more frequently in blacks. Fortunately, breast cancer is relatively uncommon in this age group.

Survival after the diagnosis of breast cancer is poorer among black patients and to a lesser extent among Hispanic patients compared to white patients. Patients who are black or Hispanic have been reported to present with a higher stage or more advanced disease. Even after adjusting for stage, survival rates were lower for blacks although not for Hispanics. These survival differences are greater at more advanced stages.

Using a group of over 6,000 breast cancer patients accrued over a 20-year period, our research at UT–San Antonio has confirmed these previous findings. Minority patients do indeed have a worse outcome. Five-year survival in whites with breast cancer was 75 percent, this decreased to 70 percent in Hispanics and 65 percent in blacks. Minorities did present with higher stage disease, and blacks—but not Hispanics—had a worse prognosis within each stage.

Since systemic hormonal or chemotherapy can improve survival for breast cancer patients, differences in the percentage of patients receiving systemic therapy would affect survival. However, evidence from our study and at least one other indicates that minority women receive systemic treatment at approximately the same frequency as whites. Thus, observed survival differences cannot be explained by different access to systemic treatment.

There are differences in breast tumor biology in whites compared with blacks and Hispanics. A number of breast tumor biologic factors known to be associated with a worse prognosis are found more commonly in minority women. Minority women are more likely to be younger at diagnosis, have larger tumors, have more lymph

node involvement, have tumors with poor histologic features, and have tumor cells that divide more rapidly and lack estrogen and progesterone receptor.

A delay in detecting the tumor could explain some of these findings—lack of screening or access to health care, or cultural beliefs and attitudes that lead to a delay in diagnosis may contribute to later detection, and therefore worse survival in minority breast cancer patients. But it is also possible that the environment associated with poverty or minority culture could result in genetic changes that lead to the more aggressive breast cancer characteristics we observe in minority women.

There are a number of established patient and tumor characteristics used to make therapeutic decisions for individual patients. These include age, menopausal status, tumor size, nodal status, ER status, histologic or microscopic features, proliferation fraction and patient attitude and choice. If these factors are known, the ethnicity of the patient adds little if any independent information to the therapeutic decisionmaking process, and I do not believe it should be used.

Because of the possible misunderstanding of the nature of clinical trials, minority women may not wish to participate in these trials. This may be the result of a number of factors including cultural differences, educational level, or mistrust of the traditional medical establishment. Additionally, the decision not to participate in a clinical trial may simply be the individual's personal choice.

All women should know that participation in current clinical trials gives the opportunity to receive the best possible therapies for breast cancer now as well as contributing to better therapies for everyone in the future. Because the average length of time needed to accrue patients of all ethnicities to cooperative group, adjuvant breast cancer trials is 4 to 5 years, it simply is not feasible to conduct separate trials for white and black women, nor is it necessary.

Along with improvement in the basic science of breast cancer pathogenesis and conduct of clinical trials applicable to all, a few simple measures can decrease mortality in minority and majority women now. Rather than implementing new, complex or costly separate research programs or special separate clinical initiatives, minority women and their nonminority counterparts should first be educated on the following points, and where appropriate, be provided the means to achieve them. This approach would provide the greatest benefit at the lowest cost.

These are the points. One, have a diet high in fruits, vegetables and complex carbohydrates like starch, but low in fat and total calories.

Two, have a low alcohol consumption.

Three, exercise regularly and vigorously.

Four, breast-feed your children, preferably for a long time.

Five, be aware of your body and practice regular breast self examinations.

Six, get a mammogram every year or two if you are 50 or older.

And seven, consult a physician immediately if there is any suspicion of breast cancer.

Breast cancer is a treatable disease and most patients can survive breast cancer. The major problem lies in determining the most

effective mechanism to get this information to minority women in a way that renders it meaningful to them——

Mr. TOWNS. I hate to cut you——

Dr. ELLEDGE. And results in change.

Mr. TOWNS. That is it? OK.

[The prepared statement of Dr. Elledge follows:]

PREPARED STATEMENT OF RICHARD M. ELLEDGE, M.D., DIVISION OF ONCOLOGY, UNIVERSITY OF TEXAS HEALTH SCIENCE CENTER

The overall incidence of breast cancer is lower in blacks and Hispanics compared with whites. A closer analysis shows that this lower incidence is seen primarily in older women-differences gradually narrow with decreasing age, until around age 40 to 45 the incidence is approximately equal. In younger women, those less than 35, breast cancer may actually occur slightly more frequently in blacks. Fortunately, breast cancer is relatively uncommon in this age group.

Survival after the diagnosis of breast cancer is poorer among black patients, and to a lesser extent among Hispanic patients, compared to white patients. Patients who are black or Hispanic have been reported to present with higher stage or more advanced disease, but even after adjusting for stage, survival rates are lower for blacks (though not for Hispanics). These survival differences are greater at more advanced stages.

Using a group of over 6000 breast cancer patients accrued over a 20 year period, our research at UT San Antonio has confirmed these previous findings. Minority patients do indeed have a worse outcome. Five year survival in whites with breast cancer was 75%; this decreased to 70% in Hispanics, and 65% in blacks. Minorities did present with higher stage disease, and blacks (but not Hispanics) did have a worse prognosis within each stage.

Since systemic hormonal or chemotherapy can improve survival for breast cancer patients, differences in the percentage of patients receiving systemic therapy would affect survival. However, evidence from our study and at least one other indicates that minority women receive systemic treatment at approximately the same frequency as whites. Thus, the observed survival differences cannot be explained by different access to systemic treatment.

There are differences in breast tumor biology in whites, compared with blacks and Hispanics. A number of tumor biologic factors known to be associated with a worse prognosis are found more commonly in minority women. Minorities are more likely to be younger at diagnosis, have larger tumors, have more lymph node involvement, have tumors with poorer histologic (microscopic) features, and have tumor cells that divide more rapidly and lack estrogen and progesterone receptor. A delay in detecting the tumor could explain some of these findings—lack of screening or access to health care, or cultural beliefs and attitudes that lead to a delay in diagnosis may contribute to later detection and therefore worse survival in minority breast cancer patients. But it is also possible that the environment associated with poverty or minority culture could result in genetic changes that lead to the more aggressive breast cancer characteristics which we observe in minority women.

There are a number of established patient and tumor characteristics used to make therapeutic decisions for individual patients. These include age, menopausal status, tumor size, nodal status, ER status, histologic features, proliferation fraction, and patient attitude and choice. If these factors are known, the ethnicity of the patient adds little if any independent information to the therapeutic decision-making process, and I do not believe it should be used.

Because of a possible misunderstanding of the nature of clinical trials, minority women may not wish to participate in these trials. This may be the result of a number of factors, including cultural differences, educational level, or mistrust of the traditional medical establishment. Additionally, the decision not to participate in a clinical trial may simply be the individual's personal choice. All women should know that participation in current clinical trials provides the opportunity to receive the best possible therapies for breast cancer now, as well as contributing to better therapies for everyone in the future. Because the average length of time needed to accrue patients of all ethnicities to cooperative group, adjuvant breast cancer trials is 4 to 5 years, it simply is not feasible to conduct separate trials for white and black women, nor is it necessary.

Along with improvement in the basic science of breast cancer pathogenesis, and conduct of clinical trials applicable to all, a few simple measures can decrease breast cancer mortality in minority—and majority—women now. Rather than implementing new complex or costly separate research programs or special, separate clinical

initiatives, minority women (and their non-minority counterparts) should first be educated on the following points and, where appropriate, be provided the means to achieve them. This approach would provide the greatest benefit for the lowest cost. These are the points:

1) Have a diet high in fruits, vegetables, and complex carbohydrates (like starch), but low in fat and total calories.
2) Have a low alcohol consumption.
3) Exercise regularly and vigorously.
4) Breast feed your children, preferably for a long time.
5) Be aware of your body and practice regular breast self exam.
6) Get a mammogram every year or two if you are 50 or older.
7) Consult a physician immediately if there is any suspicion of breast cancer. Breast cancer is a treatable disease, and most patients can survive breast cancer.

The major problem lies in determining the most effective mechanism to get this information to minority women in a way that renders it meaningful to them and results in change.

Mr. TOWNS. I ask unanimous consent that the black and white survival study be included in the record as well as articles from this panel. No objection, so ordered. There can't be any objection because I am the only one here.

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Notes

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Tumor Biologic Factors and Breast Cancer Prognosis Among White, Hispanic, and Black Women in the United States[1]

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Background: **In the United States, prognosis and survival after the diagnosis of breast cancer is poorer among black patients and, to a lesser extent, among Hispanic patients, compared with white patients. Patients who are black or Hispanic have been reported to present with higher stage or more advanced disease. Even after adjusting for stage, however, survival rates are lower for blacks but not for Hispanics.** ***Purpose:*** **Our purpose was to compare survival, age, tumor size, nodal status, estrogen-receptor (ER) and progesterone-receptor (PgR) status, histologic type, S-phase fraction, DNA ploidy status, HER-2/neu protein expression, and p53 protein status, along with systemic treatment, in a large group of white, black, and Hispanic U.S. women.** ***Methods:*** **From 1970 to 1991, breast tumor specimens were submitted to The University of Texas Health Science Center from 31 contributing hospitals throughout the United States for ER and PgR assay. A total of 4885 white, 1016 black, and 777 Hispanic women were eligible for this study. Median follow-up was 57 months.** ***Results:*** **Overall, white women were significantly more likely to be older and to have smaller tumors, have less lymph node involvement, have tumors with positive ER and PgR status, and have a lower S-phase fraction compared with Hispanic or black women. There were no clinically important differences in DNA ploidy, histologic type, HER-2/neu, and p53 expression among the three groups. Considering all stages, white women had the best overall survival (date of diagnosis to date of death) at 5 years—75% ± 1% (means ± SE), with a median survival of 166 months, but Hispanic women had an intermediate survival—70% ± 2% (median survival, 156 months), and black women had the worst survival—65% ± 2% (median survival, 117 months) ($P<.0001$). For node-negative patients, there was no significant difference in disease-free survival (date of diagnosis to date of first recurrence) or overall survival, although blacks tended to have a worse prognosis. For node-positive or locally advanced disease and for metastatic disease, blacks had significantly ($P<.0001$) worse disease-free and overall survival than did white or Hispanic women. Differences in the use of systemic therapy did not explain these outcomes.** ***Conclusion:*** **A number of biologic factors associated with poor prognosis are found with a significantly increased frequency in breast tumors from Hispanic and, particularly, from black women. Tumors with a more aggressive biology could lead to a higher stage at diagnosis and a poorer survival for the group as a whole. [J Natl Cancer Inst 86:705-712, 1994]**

In the United States, prognosis and survival after the diagnosis of breast cancer is poorer among black patients (*1,2*) and, to a lesser extent, among Hispanic patients (*3-5*) compared with white patients. Patients who are black or Hispanic have been reported to present with higher stage or more advanced disease (*6-8*). Even after adjusting for stage, however, survival rates are lower for blacks (*9,10*) but not for Hispanics (*7*). Differences in treatment might also account for the survival differences, but black patients who received the same or similar therapy still have a worse outcome (*9,11*). Other conditions, such as the lower socioeconomic class of minority women, are also associated with a worse prognosis (*12,13*); however, the precise cause of this as-

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sociation is unknown. A delay in diagnosis related to lack of access to medical care or to cultural beliefs about cancer might contribute to a worse survival. Although intuitively this delay could explain some of these findings, at least one study (*14*) found no clinically significant interval between symptom recognition and medical consultation between white women and black women.

Differences in tumor biology have been found according to race or ethnicity. Tumors from black women and Hispanic women have been reported to have a higher rate of estrogen-receptor (ER) negativity (*7,15-17*), but two studies (*18,19*) found similar rates. Among blacks, tumors tend to be less differentiated (*17,19,20*). Two small studies (*1,8*) reported a slightly increased incidence among blacks of medullary carcinoma (*1,8*), a histologic type associated with a better prognosis, while lobular carcinoma may be less common (*20*).

Rather than socioeconomic or cultural disparity, we hypothesized that differences in tumor biology might contribute to a higher stage at diagnosis and to poorer overall survival (date of diagnosis to date of death) among minority breast cancer patients. In this study, we compared survival, age, tumor size, nodal status, ER and progesterone-receptor (PgR) status, histologic type, S-phase fraction, DNA ploidy status, HER-2/neu protein expression, and p53 protein status, along with systemic treatment, in a large group of women from throughout the United States who were white, black, or Hispanic. We believe this is the first report analyzing the distribution of more recently discovered tumor biologic factors according to patient ethnicity.

Patients and Methods

Patients

From 1970 to 1991, breast tumor specimens were submitted to our laboratory for ER and PgR assay from hospitals throughout the United States. There were 31 contributing institutions consisting of hospitals of varying sizes and with academic, private, and government affiliations. A total of 4885 white, 1016 black, and 777 Hispanic women were eligible for this study. The race or ethnicity of the patients was recorded at the participating hospitals. Asian-American women, Native-American women, and those designated as unknown were coded separately and were not included in this study. To be included, patients had to be female with a diagnosis of invasive breast cancer and have follow-up information for 6 months or more. Additionally, the following data must have been known: ethnicity, age, tumor size (except for metastatic disease), nodal status (except for metastatic or locally advanced disease), and ER status. For prognostic and clinical reasons, patients were placed in one of three stages: negative axillary nodes, positive nodes or locally advanced disease that involved the chest wall or skin, or distant metastatic disease. All follow-up was obtained by review of the medical record, tumor registry reports, or telephone contact. Histologic type and other factors were determined on subsets of patients. The patient composition of these subsets was random with regard to ethnicity. Median follow-up of patients who were alive was 57 months.

Prognostic Markers

ER and PgR were assayed using ligand binding methods on frozen tumor powder (*21-23*). ER greater than or equal to 3 fmol/mg and PgR greater than or equal to 5 fmol/mg of cytosol protein were defined as ER-positive and PgR-positive, respectively. Specimens were prepared and analyzed by DNA flow cytometry as published previously (*21*). A DNA index of 1 was diploid; other than 1 was aneuploid. The cut point defining low and high S-phase was 6.7% for diploid tumors and 11% for aneuploid tumors (*24*). Histologic type was determined in most cases by review of the pathology report or, in some cases, from patient records. HER-2/neu protein expression was determined by Western blotting (*25*). p53 protein expression was determined immunohistochemically according to the method of Allred et al. (*26*), using a cocktail of two antibodies (PAb1801 and PAb240; Novocastra Laboratories Ltd., New Castle, England). Tumors scoring 2 or greater for nuclear accumulation of p53 protein were deemed to have positive staining.

Statistical Analysis

Chi-square tests were used to compare systemic treatment rates, age, tumor size, ER status, PgR status, nodal status, S-phase fraction, DNA ploidy status, HER-2/neu expression, and p53 protein status to ethnicity. Disease-free survival (date of diagnosis to date of first recurrence) was defined as the interval between the diagnostic biopsy and the first recurrence of breast cancer. Patients who died without documented disease recurrence were considered censored for disease-free survival, but their deaths were included in the analysis of overall survival. The Kaplan–Meier product limit technique was used to estimate disease-free and overall survival curves, and the curves were compared using logrank statistics for censored data. Cox's model was used to evaluate various combinations and interactions of biologic factors in multivariate form. All computations were done with the use of Statistical Analysis System (SAS; SAS Institute Inc., Cary, N.C.) version 6 software.

Results

Differences in Survival

Of the 4885 white, 1016 black, and 777 Hispanic patients who were eligible for this study, there were highly significant differences in overall survival (Fig. 1, A). Five-year survival in all white patients with breast cancer was 75% ± 1% (means ± SE; median survival, 166 months). This 5-year survival decreased to 70% ± 2% (median, 156 months) in Hispanics and further declined to 65% ± 2% (median, 117 months) in blacks. The global P value for these findings was <.0001. When comparing only whites to Hispanics, the survival difference was also significant (P = .03). When comparing only Hispanics to blacks, the difference was also significant (P = .02). The survival of whites versus blacks was highly significant (P<.0001). Disease-free survival presented a similar pattern except that there was no significant difference between whites and Hispanics. This finding is generally consistent with survival differences reported in previous surveys of breast cancer patients. Possible reasons for this worse survival are differences in stage at diagnosis, treatment, or tumor biology.

Differences in Stage at Diagnosis

Patients were stratified as having node-negative, node-positive or locally advanced disease, or distant metastatic disease. Fifty-five percent of whites, 43% of Hispanics, and 42% of blacks presented with node-negative breast cancer (P<.0001). By logrank testing, there was no significant difference in overall survival (Fig. 1, B) or disease-free survival (data not shown) for this stage. There was, however, a trend for worse overall survival among blacks than among whites (P = .1). Only 39% of whites presented with node-positive or locally advanced disease; however, 50% and 48% of Hispanics and blacks, respectively, presented at this stage (P<.0001). There was a significant difference in overall survival among the groups (P = .008; Fig. 1, C) and in disease-free survival (P = .001; data not shown). Overall survival was not different for white versus Hispanic patients, but the difference was significant for white versus black patients (P = .002) and trended toward significance for black versus Hispanic patients (P = .056). Also, 5.4% of whites, 6.9% of Hispanics, and 9.5% of blacks presented with distant metastatic disease (P<.0001). Patterns of survival were similar to lower stages, with blacks having

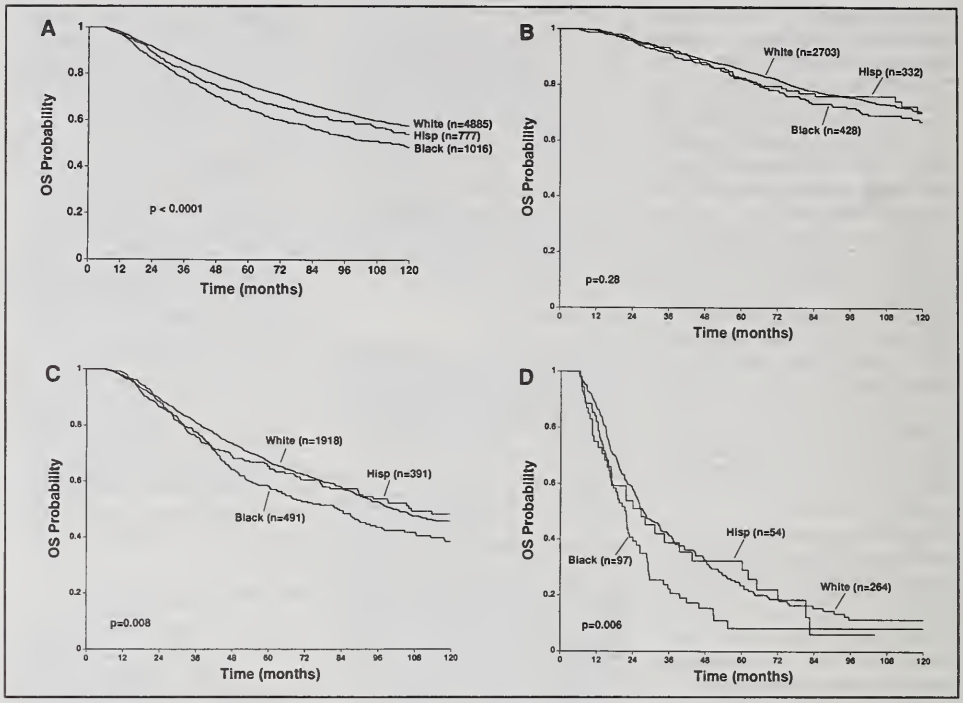

Fig. 1. Overall survival (OS) of all breast cancer patients by ethnic group. A) All stages. The 5-year overall survival for white, Hispanic (Hisp), and black patients are 75%, 70%, and 65%, respectively. B) Node-negative. C) Node-positive or locally advanced disease. D) Distant metastasis at initial presentation.

a comparatively shorter survival than whites or Hispanics (P = .006; Fig. 1, D). The median survival for whites, Hispanics, and blacks with distant metastasis was 28 months, 27 months, and 22 months, respectively. Overall, black women and Hispanic women were more likely to present with more advanced disease, and black women had a worse outcome for each stage of breast cancer. Differences in stage at diagnosis do not fully explain the worse survival in black women.

Differences in Treatment Received

The administration of systemic hormonal therapy or chemotherapy can improve disease-free and overall survival among breast cancer patients (27). Since differences in the proportion of patients receiving systemic therapy could affect survival, we examined treatment given by ethnic group (Table 1). Surprisingly, for both node-negative and node-positive cancers, Hispanic women were more likely to receive therapy by a margin of 10%-20% (P<.0001). Among blacks and whites, the likelihood of therapy was generally similar; however, for node-negative disease, 21% of whites versus 12% of blacks were treated. Although we found that whites were somewhat more likely to be systemically treated for node-negative breast cancer than blacks, this difference would have a negligible impact on survival in this stage of disease. There were no differences in the rate of systemic therapy administration for patients with distant metastasis. Thus, overall, minority women were at least as likely to be systemically treated as white women. Although dose intensity and compliance data were not available, the impact of variation in dose intensity in the range expected in this study would probably be modest or insignificant.

To eliminate any possible effect of systemic treatment, we performed separate survival analyses on untreated nonmetastatic patients only. In this specific analysis, there were 2553 white, 248 Hispanic, and 443 black patients. Most patients were in the node-negative group. Because of a reduction in patient number, some statistical power was lost, but there was no change in survival patterns compared with treated patients, thus confirming that ethnic differences were not due to treatment differences (data not shown).

We also examined the type of systemic treatment used. Whites were proportionately more likely to receive endocrine therapy than chemotherapy, compared

Table 1. Comparison of treatment and tumor biologic factors according to ethnic status

	White		Hispanic		Black	
	%	No.	%	No.	%	No.
Systemic therapy						
Node-negative	21.0	2641	39.9	323	12.1	405
Node-positive or locally advanced disease	74.1	1914	85.1	390	81.3	497
Metastatic disease	93.0	259	92.5	53	90.6	96
Age, y						
<35	2.8	136	6.2	48	6.3	64
35-50	21.1	1031	32.8	255	31.1	316
>50	76.1	3718	61	474	62.6	636
Tumor size, cm						
≤2	44.5	2147	32.1	246	29.7	294
2.1-5	44.6	2150	51.3	393	42.6	422
>5	10.9	525	16.6	127	27.7	275
Nodal status						
0	57.9	2721	45.9	335	48.8	434
1-3	21.1	992	24.1	176	24.6	219
>4	21	989	30.0	219	26.6	237
ER status						
Positive	77.9	3807	70.1	545	62.1	631
Negative	22.1	1078	29.9	232	37.9	385
PgR status						
Positive	56.0	2331	50.6	360	40.8	357
Negative	44.0	1833	49.4	352	59.2	517
S-phase fraction						
High	38.5	577	48.4	155	49.4	130
Low	61.5	923	51.6	165	50.6	133
Median	6.9	—	8.3	—	8.6	—
HER-2/neu protein						
Positive	16.1	84	20.9	14	13.8	15
Negative	83.9	439	79.1	53	86.2	94
p53 protein						
Positive	50.9	473	54.2	90	54.9	100
Negative	49.1	457	45.8	76	45.1	82

	P value		
	White versus black	White versus Hispanic	Hispanic versus black
Age	<.0001	<.0001	.74
Tumor size	<.0001	<.0001	<.0001
Nodal status	<.0001	<.0001	.31
ER status	<.0001	<.0001	<.0001
PgR status	<.0001	.007	<.0001
S-phase fraction	.001	.001	.81
HER-2/neu protein	.55	.32	.21
p53 protein	.31	.42	.89

with the other two groups ($P<.0001$). Stratification by receptor status demonstrates that this was due to a higher rate of receptor positivity among whites.

Differences in Biologic Factors

We next investigated differences in tumor biologic features, which might also account for the disparate survivals. There were statistically significant differences in age, tumor size, and nodal status among the three groups that are consistent with results of other smaller, previously published studies (*2,12,13*). There was a greater percentage of minority women aged 50 years or younger among both Hispanics and blacks ($P<.0001$; Table 1). Whites had a greater proportion of tumors less than or equal to 2 cm than did blacks or Hispanics; however, minorities, especially blacks, had relatively more tumors greater than 5 cm. Black and Hispanic women were also more likely to be node-positive and to have more positive nodes (Table 1).

The histologic types of breast cancer were distributed very evenly among the 6583 patients analyzed (data on histologic type was not available for 95 patients). Eight-four percent of whites, 82% of Hispanics, and 81% of blacks had infiltrating ductal carcinoma. Medullary carcinoma was found at twice the frequency in blacks compared with whites (5.2% versus 2.6%, respectively). The incidence of lobular carcinoma was not different among blacks and whites, contrary to a previous report (*20*).

Table 1 shows the ER and PgR status according to the ethnicity of the patient. White women had the highest rate of ER positivity (78%). This proportion dropped to 70% for Hispanic women and to 62% for black women ($P<.0001$). Similar results were also seen for PgR, with white women having 56% PgR-positive tumors, Hispanic women 51%, and black women 41%. Because age and menopausal status heavily influence receptor status and because black patients and Hispanic patients tended to be younger, ER and PgR were stratified by age and race (Fig. 2). For women younger than 35 years, there was no significant difference in ER or PgR status by ethnicity, although younger black patients tended to have a higher incidence of ER-positive tumors. The number of patients in this age category was small, which could prevent an actual difference from being detected. Among women between the ages of 35 and 50 years or those older than 50 years, whites had the highest percentage of ER- and PgR-positive tumors, followed by Hispanics and then blacks ($P<.0001$).

S-phase fraction (an important prognostic factor) was determined, along with DNA ploidy status, by flow cytometry (Table 1). Fewer whites had high S-phase fraction (38.5%) than Hispanics (48.4%) or blacks (49.4%) ($P<.0001$). The median S-phase fraction was 6.9% for whites, 8.3% for Hispanics, and 8.6% for blacks. There were no clinically important differences in DNA ploidy status found among the three groups in an analysis of 2471 tumors.

Molecular genetic markers can be used to define subsets of breast cancer patients with different risks of recurrence and possibly different etiologies. Two molecular markers, the HER-2/neu oncogene and the p53 (also known as TP53) tumor suppressor gene, were assayed in these breast tumors (Table 1). HER-2/neu

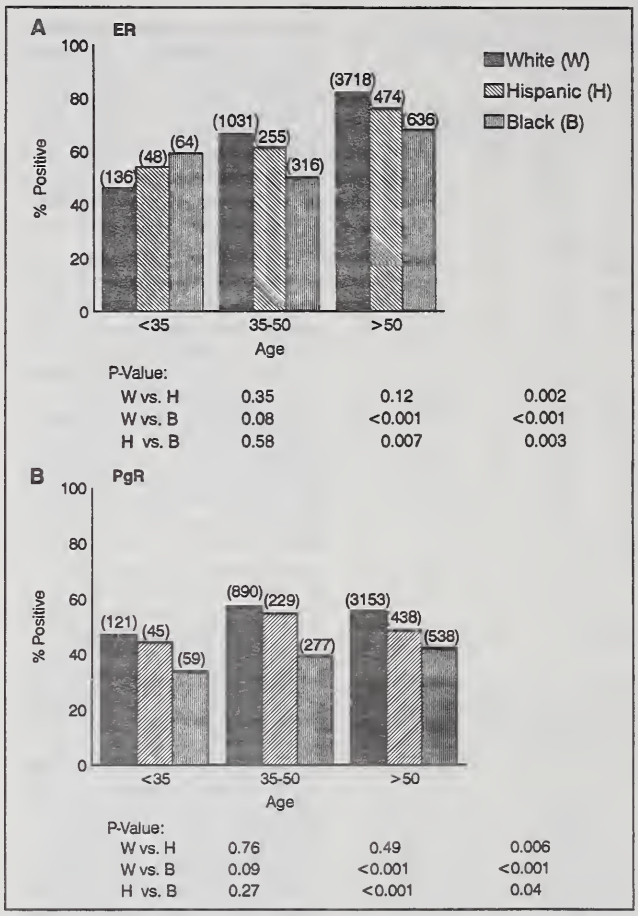

Fig. 2. Steroid receptor status by age in years and ethnic group. A) Estrogen receptor (ER). B) Progesterone receptor (PgR). Numbers in parentheses = total number of patients.

protein expression was measured by Western blotting. Nuclear accumulation of p53 protein which, in most but not all cases, represents mutational inactivation of the gene (*28*), was detected immunohistochemically. No significant differences by race were evident, and when HER-2/neu and p53 protein status were further subdivided by nodal involvement and ethnicity, no differences emerged (data not shown).

To investigate the relative and independent contribution of ethnicity to overall survival, univariate and multivariate analyses were performed (Table 2). In the univariate analyses, stage and receptor status were prognostic for survival. Black race was also a significant prognostic factor. Ethnicity was included in multivariate analyses, using two indicator variables that considered whites as the comparison group. Black race lost some of its prognostic relevance when the contribution of other variables was considered. Its independent contribution to predicting overall survival was significant but not as strong. The relative risk of death for patients of black race was 1.2 (95% confidence interval = 1.1-1.4; P = .004). Thus, after considering stage and receptor status, a relative increase in the odds of death for black women with breast cancer compared with white and Hispanic women is apparent but small. Ethnicity was not an independent factor predicting survival when evaluating only Hispanic and white patients, but being black independently predicted survival when compared separately with either Hispanics or whites. We performed a second survival analysis by inserting size into the model and by deleting all patients with distant metastases because tumor size was unknown for many of these women. Tumor size became the second most powerful prognostic indicator after stage. Black race remained a significant factor. No other changes were seen. S-phase was not included in these models, since this would have resulted in the loss of a substantial number of patients.

Discussion

In this study, we found that overall survival for breast cancer patients who were black or Hispanic was significantly worse than for those who were white. Minority women were more likely to present with clinically advanced disease. Stage for stage, however, two trends emerged. Blacks still had a worse prognosis, and the prognosis for Hispanics and whites in each stage did not differ significantly. These results support the belief that minority women, especially blacks, have a worse prognosis. Other studies have shown that blacks have a worse prognosis overall (*1,2,4,12*), a worse prognosis within each stage (*1,2,10*), and present with more advanced disease (*6,8*). A slightly worse survival rate has also been noted for Hispanic patients (*4,12*) relative to white patients (about 2%-5% at 5 years).

There are several possibilities for this poorer prognosis and more advanced disease. First, there could be a longer interval before receiving or seeking treatment,

Table 2. Survival analyses (n = 5750)

Variable	Univariate *P*	Multivariate *P*	Relative risk
Stage	<.0001	<.0001	2.9
Estrogen receptor status, negative versus positive	<.0001	<.0001	1.4
Progesterone receptor status, negative versus positive	<.0001	<.0001	1.4
Age, <50 versus ≥50, y	.017	<.0001	1.3
Black versus white and Hispanic	<.0001	.004	1.2
Hispanic versus white and black	.3	.14	—

resulting in a larger window of opportunity for tumor growth and metastatic spread and a more advanced stage at diagnosis. But this longer interval does not explain the observation that blacks still have a worse prognosis stage for stage. Also, at least three studies have examined the possibility that a longer interval might influence the stage at presentation. Coates et al. (*14*) found no clinically significant interval between symptom recognition and medical consultation between white and black patients, but a study from The University of Texas M. D. Anderson Cancer Center, Houston (*12*), concluded that a delay in seeking treatment did not explain ethnic differences in survival in breast cancer patients. In a third study (*29*), the time between recognition of symptoms and seeking medical attention was similar for blacks and whites. Thus, published evidence does not support the idea that a longer time exists between symptom recognition and treatment or that, if it does, survival would be affected. If minority women were experiencing a delay in diagnosis for any reason, their age at diagnosis might tend to be older not younger, as was found.

A second possibility for ethnic differences in survival could be due to treatment. In the present study, we found that overall, black women and Hispanic women were at least as likely to receive systemic adjuvant therapy as were white women; however, within the node-negative group, black women received therapy less often. Results of the National Cancer Institute Black/White Cancer Survival Study (*30*) also showed that blacks and whites received systemic adjuvant therapy for node-positive breast cancer at a similar frequency. Also, despite the same stage and similar therapy, blacks are reported to still have a worse outcome after systemic (*11*) or local treatments (*9*).

A third possibility could explain these divergent outcomes. Our data suggest that differences in intrinsic biologic characteristics of tumors among Hispanics and blacks could contribute to a worse prognosis. Minority women were more likely to be younger at diagnosis, and overall tumors from minority women were more likely to be ER and PgR negative and to have a higher proliferative fraction. Although blacks did have a greater incidence of ER negativity, in a small subset of patients (those <35 years old) blacks tended to have a lower rate of ER negativity. This lower rate may be because of the small size of this subset. All three of these latter factors are associated with more aggressive tumors (*24,31-33*) and could contribute to a more advanced stage of disease and a worse prognosis. Tumors with a higher proliferative rate are more likely to be larger at diagnosis (*34*) and would be expected to become clinically evident at a younger age. Other small studies have also found a lower incidence of ER and PgR among blacks (*15,16*) and Hispanics (*7*), but this is the first study, to our knowledge, to find a higher proliferative rate associated with tumors from Hispanic women and black women. Thus, tumors from both black patients and Hispanic patients were associated with several adverse biologic factors and both groups had a worse prognosis overall. Hispanic patients, however, did not have a worse prognosis stage for stage than white patients. Black patients, however, did have a worse prognosis overall and stage for stage. This finding suggests that additional biologic and other factors associated with black race result in a relatively higher breast cancer mortality, even within stages.

Molecular events are now being used as tools to help define the epidemiology and inciting events of particular tumors in certain populations (*35*). We examined two molecular markers in relation to race, the p53 tumor suppressor gene and the HER-2/neu oncogene. Mutations of the p53 gene were searched for indirectly by measuring nuclear accumulation of p53 protein immunohistochemically. In most, but not all instances, this accumulation is the result of a gene mutation, and it is associated with a higher rate of recurrence (*26*). There were no significant differences in the rate of p53 mutation, as detected by nuclear accumulation of protein among ethnic groups. This finding does not mean, however, that specific mutational patterns or types of mutation might exist in each group, reflecting varied breast cancer etiologies in different races. For the other molecular marker, HER-2/neu, there were no significant differences in the frequency of overexpression, an event linked to a higher likelihood of recurrence in breast cancer (*25*).

There were other factors measured that were similar in the three ethnic groups. DNA ploidy status, a reflection of gross genetic stability or change, was not substantially different in the three groups. There were no clinically significant differences in histologic type, although there was a twofold greater proportion of medullary tumors among blacks. The absolute magnitude of this difference, 2.6% versus 5.2%, is small and has minor clinical significance; however, it reflects a different tumor biology.

There are several potential limitations of this study. First, there might have been a selection bias caused by referral patterns that resulted from the availability of special prognostic factor assays at this institution. However, tumors were sent only to measure ER, a test widely available and done commercially. Additionally, this was a multi-institutional trial with 31 participating centers. Second, because no formal, specific definition of race or ethnicity was used, misclassification could have occurred. Race or ethnicity was determined by investigators at each institution. This determination was done on the basis of appearance, patient questioning, surname, or medical record review. The possible extent of misclassification or impact on our findings is difficult to quantitate but would seem unlikely to produce a consistent effect. Third, follow-up could vary according to ethnic group

for such reasons as poor compliance. However, the main end point in this study was patient mortality, which should not be substantially influenced by differential follow-up. We analyzed the median follow-up of patients remaining alive by ethnic group. This median follow-up was 58 months for whites, 56 months for blacks, and 48 months for Hispanics. The somewhat shorter median follow-up for Hispanics could result in fewer events being detected and a slightly better survival than would have been seen with an additional 10-12 months of follow-up. Fourth, the extent of staging workup was not controlled, and it is possible that minorities were more frequently understaged. However, studies have shown that extensive staging procedures for stage I and II breast cancer rarely result in a finding of metastatic disease if history, physical examination, biochemical parameters, and chest x ray are unremarkable (*36*). The majority of nonmetastatic patients in this study were in this category, but we cannot exclude the possibility that a small fraction of patients with node-positive or locally advanced disease actually had gross metastatic disease that was not detected and that this understaging might have occurred more often in minorities. However, if differential understaging did occur, it is difficult to explain why it would apply to blacks, who had worse survival within stages, but not to Hispanics. Fifth, lack of mammographic screening could result in a higher stage at diagnosis for minorities. Information on mammographic screening was not available for this analysis. However, many of the women in this study were entered prior to the more widespread use of mammography. Finally, information on socioeconomic status would be useful in determining its role in breast cancer morbidity, but these data were not collected.

In summary, we have observed a poorer overall survival among breast cancer patients who were black or Hispanic. Differences in stage at diagnosis or use of systemic treatment are unlikely to fully explain these differences. A number of biologic factors associated with a poor prognosis were found, with a significantly increased frequency in breast tumors from Hispanic women and, particularly, from black women. Tumors with a more aggressive biology could lead to a higher stage at diagnosis and a poorer survival for the group as a whole. The environment associated with poverty or minority cultures may result in genetic changes that lead to a more aggressive type of breast cancer, especially in its earlier or preclinical stages. However, other reasons, in addition to this more aggressive tumor phenotype, may contribute to the modestly worse prognosis for black women and for Hispanic women with breast cancer.

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Notes

[1]Editor's note: This paper cites one or more National Surgical Adjuvant Breast and Bowel Project (NSABP) clinical trials, to which some falsified data were submitted. Insofar as we are able to determine, impeached data do not alter the conclusions of any of the studies. Reanalyses of data from several of the trials are available through the National Cancer Institute's CancerFax and CancerNet.

To access CancerFax, call 301-402-5874 from the telephone on your fax machine, and when prompted for the six-digit code, enter 400027 (for trial B-06) or 400028 (for trials B-13/B-14). Follow the voice prompts to receive the information. To access CancerNet, send an electronic mail message to cancernet@icicb.nci.nih.gov with cn-400027 (for trial B-06) and/or cn-400028 (for trials B-13/B-14) in the body of the message (if requesting both, enter the codes on separate lines). The items will be returned to you via electronic mail, usually within 10 minutes.

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Acetylator Phenotype, Aminobiphenyl–Hemoglobin Adduct Levels, and Bladder Cancer Risk in White, Black, and Asian Men in Los Angeles, California

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Background: **There is a large body of epidemiologic and experimental data that have identified a number of arylamines as human bladder carcinogens. Metabolic activation is required to biotransform these arylamines into their carcinogenic forms, and N-hydroxylation, which is catalyzed by the hepatic cytochrome P4501A2 isoenzyme, is generally viewed as the first critical step. On the other hand, the N-acetylation reaction, catalyzed by the hepatic *N*-acetyltransferase enzyme, represents a detoxification pathway for such compounds. The *N*-acetyltransferase enzyme is coded by a single gene displaying two phenotypes, slow and rapid acetylators. In the United States, cigarette smoking is a major cause of bladder cancer in men, and carcinogenic arylamines present in cigarette smoke are believed to be responsible for inducing bladder cancer in smokers.** ***Purpose:*** **Our purpose was to test the differences in three ethnic/racial groups for the prevalence of acetylator phenotypes and to ascertain whether slow acetylators actually have higher levels of activated arylamines in comparison with rapid acetylators.** ***Methods:*** **One hundred thirty-three male residents of Los Angeles County who were either white, black, or Asian (Chinese or Japanese) and over the age of 35 years were assessed for their acetylator phenotype and levels of 3- and 4-aminobiphenyl (ABP) hemoglobin adducts. Subjects were either lifetime nonsmokers (n = 72) or current cigarette smokers of varying intensity (n = 61).** ***Results:*** **The proportion of slow acetylators was highest among whites (54%), intermediate among blacks (34%), and lowest among Asians (14%). Similarly, geometric mean levels of both 3- and 4-ABP–hemoglobin adducts were highest in whites (1.80 and 49.2 pg/g hemoglobin [Hb], respectively), intermediate in blacks (1.54 and 38.5 pg/g Hb), and lowest in Asians (0.73 and 36.0 pg/g Hb). As expected, cigarette smokers had significantly higher mean levels of both 3- and 4-ABP–hemoglobin adducts relative to nonsmokers, and the levels increased with the number of cigarettes smoked per day (*P*<.0005 for both adducts). Slow acetylators consistently exhibited higher mean levels of ABP–hemoglobin adducts relative to rapid acetylators, independent of race and level of smoking.** ***Conclusion:*** **The present cross-sectional survey supports acetylation phenotype as an important determinant of bladder cancer risk and a possible major factor in the varying bladder cancer risk among whites, blacks, and Asians. [J Natl Cancer Inst 86:712-716, 1994]**

There is a large body of epidemiologic and experimental data in support of a number of arylamines, including 2-naphthylamine and 3- and 4-aminobiphenyl (ABP), as human bladder carcinogens. The epidemiologic data were derived mainly from studies of workers exposed to these industrial chemicals in occupational settings (*1*). Metabolic activation is required to biotransform these arylamines into their carcinogenic forms, and N-hydroxylation, which is catalyzed by the hepatic cytochrome P4501A2 isoenzyme,

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See "Notes" section following "References."

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Histological Characteristics of Breast Carcinoma in Blacks and Whites[1]

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Abstract

Tumor characteristics of 963 newly diagnosed invasive breast cancer cases from the population-based Black/White Cancer Survival Study were evaluated. Representative slides of the tumors were requested from all participating hospitals of three metropolitan areas and reviewed by one expert pathologist, blinded in regard to the age and race of patients. Nine tumor characteristics were evaluated for black and white patients. After adjusting for age, stage, and metropolitan area, blacks were significantly more likely to have high grade nuclear atypia [odds ratio (OR) = 1.97, 95% confidence interval (CI) = 1.27–3.04]; high mitotic activity (OR = 2.05, 95% CI = 1.34–3.14), grade 3 tumors (OR = 1.58, 95% CI = 1.02–2.45), and more necrosis (OR = 1.51, 95% CI = 1.16–1.98); and less likely to have well defined tubular formation (OR = 0.57, 95% CI = 0.42–0.77), marked fibrosis (OR = 0.65, 95% CI = 0.45–0.94), and positive estrogen receptor status (OR = 0.78, 95% CI = 0.58–1.05). These black/white differences remained after controlling for socioeconomic status (SES), body mass index, use of alcohol and tobacco, reproductive experience, and health care access and utilization. No significant racial differences were found for blood vessel invasion and lymphatic invasion. Although white women of high SES had more favorable tumors than those of low SES, the same pattern was not observed for blacks. High SES black women had statistically nonsignificant elevated ORs of a high mitotic index and tumor grade. These racial differences in tumor biology may have etiological and clinical implications.

Introduction

A significant B/W[3] difference in survival for women with breast cancer has been observed in the United States since the 1950s (1–5). The 5-year relative survival rates for all stages combined were 62% in blacks and 79% in whites for the period of 1983–1988 (5). Although the unfavorable survival for black patients is in part a result of a higher proportion of advanced or nonlocalized disease at the time of diagnosis, racial differences remain even after adjusting for stage or when within stage comparisons are made (5–7).

Several explanations have been suggested for the B/W disparity in survival. Numerous studies have found SES to be the main determinant of survival differences among cancer patients (8–11). Other studies have shown that black patients are less likely to have aggressive therapies and cancer-directed treatments (7, 12). Additional hypotheses include limited access to health care and more prevalent comorbidity among black women (13, 14). Differences in tumor biology between black and white breast cancer patients also have been hypothesized to play a role in the observed survival differences. Black women with breast cancer tend to have more aggressive types of tumors (15, 16). Mohla *et al.* (15) evaluated breast carcinoma of 146 black women and found significantly higher proportions of poorly differentiated tumor (55.5%) and negative estrogen receptor (42%) than those reported previously for white patients. Ownby *et al.* (16), when comparing 73 black and 1005 white patients with breast cancer from Detroit, also observed that blacks were more likely to have high grade tumors. Patients with estrogen receptor-negative and high grade tumors have shorter survival times (17, 18).

The National Cancer Institute collaborative Black/White Cancer Survival Study was implemented in 1984 to explore the reasons for the poorer survival in blacks, including social, behavioral, cultural, and clinical factors, as well as access to health care delivery and tumor biology. The study includes 1222 women with newly diagnosed breast cancer. Because the study is population based and multicenter, it is expected that black patients in the study are representative of those from urban areas of the south and west United States. The tumors were reviewed centrally and

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[3] The abbreviations used are: B/W, black/white; SES, socioeconomic status; OR, odds ratio; CI, confidence interval.

evaluated uniformly. This report examines the tumor characteristics of breast carcinoma by race and the possible reasons for these differences.

Material and Methods

Study Population. Black and white women, aged 20–79, who were residents of metropolitan areas of Atlanta, New Orleans, and San Francisco-Oakland, were eligible for the Black/White Cancer Survival Study if they were diagnosed histologically with breast cancer between January 1, 1985 and December 31, 1986. Approximately 70% of eligible black women were selected randomly for inclusion. Because blacks tend to be younger than whites at diagnosis, an attempt was made to balance the accrual of patients by age. Sampling fractions for white patients varied by age group, study center, and time period depending on the availability of cases. Approximately equal numbers of white and black women were selected for inclusion in the study. A detailed description of the study objectives and design has been published previously (13).

The study population for this report consisted of women with invasive breast cancer from whom the tumor characteristics have been evaluated by the central pathologist. The 92 women (37 black and 55 white) with carcinoma *in situ* were excluded; these tumors often have insufficient tissue for the detailed evaluation of all nine histological parameters included in this study. An additional 65 women (39 black and 26 white) were excluded because their breast cancer could not be staged. Of the remaining 1065 invasive cases with known stage, 102 (67 black and 35 white) did not have slides sent for central pathology review (Table 1). This resulted in 963 women in the final analysis, 506 black and 457 white.

Data Collection. Data were collected from three sources: abstracts of hospital medical records, in-person interview, and a central pathology review of the tumor. A breast cancer summary stage was assigned to each patient based on all available medical information using the international tumor-nodes-metastasis system (19). Details of the staging procedure were described elsewhere (14).

Information on SES was obtained from patient interview, including marital status, education, usual occupation, and total household income. A poverty index was created to adjust total household income for the number of people supported by that income. For a given number of people supported, the household income was divided by the national 1986 poverty level income for that size (20). Self-reported weight and height were used to create a body mass index (weight [kg]/height $[m]^2$). Study subjects were then categorized into less than 25th percentile, 25th to 49th percentile, 50th to 84th percentile, and 85th percentile and above for women aged 20–29 in the Second National Health and Nutrition Examination Survey (21). The last category (85th percentile) is used commonly in defining overweight for women of all ages. Alcohol consumption during the 5 years before diagnosis was collected and coded to number of drinks/day. Information on duration and amount of cigarette smoked was collected and women were classified as nonsmokers, ex-smokers, and current smokers. Data on parity, usual source of care, and insurance coverage were obtained from interviews. Patients who used hospital outpatient clinics or emergency rooms routinely were classified as not having a usual source of care. Women with Medicare or Medicaid only were included in the "public" category of type of health insurance, whereas the "private" category included women with health maintenance organizations.

Information on tumor histological type and estrogen receptor status was abstracted from hospital records. In addition, representative slides of biopsy and surgical specimens for each patient were requested from all participating hospitals and sent to one pathologist (R. J. K.) for uniform review. The pathologist was blinded in regard to race and age of the patient. The tumor was evaluated by the following pathological parameters: histological grade (1, well differentiated; 2, moderately differentiated; and 3, poorly differentiated or undifferentiated), blood vessel invasion (yes, no), lymphatic invasion (yes, no), necrosis (none, mild, moderate, marked), fibrosis (none, mild, moderate, marked), and cell reaction to tumor (none, mild, moderate, marked). Histological grade was based on tumor differentiation parameters derived from the subjective evaluation of nuclear atypia, tubular formation, and mitotic activity, each of which was assigned a score of grade 1–3 (22). For nuclear atypia, tumors in which nuclei were regular and showed little variation in size and shape were categorized as low grade or grade 1, whereas tumors with marked variation and very large, bizarre nuclei or with multiple nucleoli were categorized as high grade or grade 3. Intermediate category tumors were assigned grade 2. For tubular formation, a score of 1–3 was assigned ranging from no or few tubules (score 1) to well formed tubules with clearly visible lumina (score 3). Lobular carcinomas were excluded from the evaluation of tubular formation. For mitotic activity, tumors were scored from 1 (low) to 3 (high) based on subjective estimation rather than the exact count of mitoses/microscopic field.

Statistical Analysis. Associations between race and variables of interest were estimated by unadjusted ORs and 95% CIs (23). To evaluate the association of tumor characteristics and race, logistic regression analyses also were used to calculate ORs. These ratios represented the odds that black women with invasive breast cancer in our study had a given category of tumor characteristics relative to the odds for white women. Because age and metropolitan area were design variables and stage of disease was associated with tumor characteristics, all ORs also were adjusted for age, metropolitan area, and summary stage.

For the tumor characteristics that showed significant B/W differences in the initial analysis, selected groups of factors, including SES, lifestyle, reproductive experience, and health care access and utilizations, were examined for their contribution to the B/W tumor disparity. These factor groups were added sequentially to a polychotomous ordinal logistic model (24) using the SAS statistical program LOGISTIC Procedure (25). For an ordinal response, a test of the parallel lines assumption was performed for assessing whether a proportional odds model was appropriate for the data. The goodness-of-fit of the models were evaluated by Hosmer-Lemeshow test. Finally, the association of SES and tumor characteristics was further examined in blacks and whites separately.

Results

Of the total sample eligible for the pathology study (n = 1065), slides for 963 cases (90.4%) were evaluated. Patients for whom no pathology review was made were more likely to be black, older (ages 65–79), residents of San Francisco or with stage IV diseases (Table 1), but none of the differences were significant at the 0.05 level.

Table 1 Distributioin of total patients eligible for pathology study and those included in pathology review

Characteristics	Total eligible patients n = 1065	Pathology review sample	
		n = 963	% of total
Race			
Blacks	573	506	88.3
Whites	492	457	92.9
Age at diagnosis (years)			
20–49	416	380	91.3
50–64	372	340	91.4
65–79	277	243	87.7
Metropolitan area			
Atlanta	404	366	90.6
New Orleans	286	265	92.7
San Francisco/Oakland	375	332	88.5
Stage of disease			
I	288	265	92.0
II (no)[a]	206	185	89.8
II (n1)[b]	305	277	90.8
III	193	172	89.1
IV	73	64	87.7

[a] (no), lymph node involvement.
[b] (n1), lymph nodes involved.

Black and white patients included in this analysis were quite different from each other (Table 2). Clinically, blacks had larger tumor size, more distant metastasis, and more advanced invasive breast cancer, with ORs of 3.0 and 2.6 for stages III and IV disease, respectively, as compared with whites. In addition, they were more likely to be residents of the Atlanta metropolitan area, less likely to be married, had fewer years of education, and were poorer as measured by poverty index. Black women were more likely than whites to be employed in a "service" occupation, which was predominantly house cleaning (OR = 15.9). Over 40% of blacks (42.7%) were overweight, compared with 13.9% of whites; blacks were also younger at first pregnancy and had more children. Although black women were more likely than white women to be current smokers, they drank less frequently. Black patients used public clinics more often as their usual source of care and were more likely to have either no insurance or public insurance.

The predominant histological type of breast carcinoma in this review was ductal carcinoma, accounting for 86.3% of total cases. Other histological types were lobular (3.8%), medullary (2.5%), mucinous (2.2%), and less than 1% each for tubular, papillary, and other type. About 2% (2.3%) were mixed tumors and 1.3% inflammatory carcinoma. These histological types did not exhibit a statistically significant difference by race or estrogen receptor status.

Table 3 compares the tumor characteristics in black and white women, providing the numbers of cases, the percentage for each category, the B/W ORs, and ORs adjusted for age, metropolitan area, and stage. The ORs for both nuclear atypia and mitotic activity display a linear increase, indicating a dose-response type of relationship in which higher proportions of black women have tumors with more aggressive nuclear characteristics. An inverse trend is observed for tubular formation, which is less marked in blacks than in whites. These patterns are well reflected in the tumor grade, which integrates the different independent parameters of tumor differentiation. It becomes apparent that being black increases the odds of having higher grades: 1.19 for grade 2 (95% CI = 0.87–1.64) and 1.58 for grade 3 (95% CI = 1.02–2.45).

Another indicator of tumor differentiation, the presence of estrogen receptors, is also significantly less frequent in blacks, 55.5% *versus* 63.3% in whites (Table 3). The odds of having positive estrogen receptor tumor in black patients was 0.72 (95% CI = 0.55–0.96). After adjusting for age and stage, the OR increased to 0.78 and became borderline significant.

The capacity of the tumor to invade either blood vessels or lymph vessels or both is similar in both races. However, blacks are about 50% more likely to have any necrosis in the tumor after controlling for age, location, and stage (OR = 1.51, 95% CI = 1.16–1.98). Necrosis may reflect the adequacy of blood supply to the tumor.

The reaction of the host to the tumor is reflected in the proliferation of fibrous tissue (fibrosis) and the infiltration by white blood cells. A significant deficit in reactive fibrosis is observed in blacks, with ORs of 0.59 and 0.65 for moderate and marked fibrosis, respectively. By contrast, the infiltration by white blood cells (cell reaction) is more marked in blacks, perhaps related to tumor necrosis. When tumor size, number of positive lymph nodes, and distant metastasis were used instead of summary stage to adjust for stage of disease, the results remained unchanged.

For the histological parameters of the tumors that showed significant B/W differences, namely nuclear atypia, mitotic activity, tubular formation, grade, fibrosis, and necrosis, as well as estrogen receptor status, we examined their relationship with variables of interest. Four groups of factors that were significantly different between black and white patients and related to tumor characteristics were selected and examined, namely, SES, host factors and lifestyle, reproductive experience, and health care access and utilization. The ORs for each of the histological parameters were calculated using the polychotomous ordinal logistic regression. In Table 4, the first model shows crude ORs, indicating an increased risk of high nuclear atypia, mitotic activity, grade, and necrosis, as well as a decreased risk of tubular formation and fibrosis associated with being black. Subsequent models show how these ORs, either elevated or reduced, did not change substantially after adjusting successively for design variables (age, stage, and location), groups of SES factors (marital status, education, poverty index, and occupation), host factor and lifestyle (body mass index, smoking, and alcohol consumption), reproductive factors (parity, age at first pregnancy), and health care access and utilization (usual source of care and insurance coverage). It is apparent that the determinants of the risk for poor prognostic tumor characteristics in black women are not driven totally by the social and lifestyle characteristics of the subjects.

SES not only can reflect the economic level of an individual, but may also be used as a surrogate of some variables that are more difficult to measure, such as host immunocompetence. We selected the poverty index as an indicator of SES and further examined its association with tumor characteristics. In this analysis, we encountered the problem of uneven distribution of poverty index by race; very few white women were at the lower end of the SES scale and relatively few black women were at the upper end. When the conventional low cutpoint for dichotomy is chosen (poverty index = 125), it cannot discriminate differences in the distribution of tumor characteristics between the two

Table 2 Distributions of selected characteristics among invasive breast cancer patients by race

Variables	Black (n = 506)		White (n =457)		OR	95% CI
	n	%[a]	n	%		
General						
Age at diagnosis (years)						
20–49	203	40.1	177	38.7	1.00	
50–64	174	34.4	166	36.3	0.91	0.68–1.23
65–79	129	25.5	114	25.0	0.99	0.71–1.36
Metropolitan area						
Atlanta	208	41.1	158	34.6	1.00	
New Orleans	119	23.5	146	32.0	0.62	0.45–0.85
San Francisco/Oakland	179	35.4	153	33.5	0.89	0.66–1.20
Clinical factors						
Stage						
I	100	19.8	165	36.1	1.00	
II (no)	113	22.3	72	15.8	2.59	1.76–3.81
II (n1)	143	28.3	134	29.3	1.76	1.25–2.48
III	111	21.9	61	13.4	3.00	2.01–4.48
IV	39	7.7	25	5.5	2.57	1.47–4.51
Primary Tumor (T)						
T-1	147	29.1	217	47.7	1.00	
T-2	233	46.1	168	36.9	1.43	1.24–1.65
T-3	60	11.9	37	8.1	1.34	1.15–1.56
T-4	65	12.9	33	7.3	1.31	1.16–1.47
Unknown	2	(0.0)[b]	1	(0.0)		
No. of positive nodes						
0	230	50.9	253	58.6	1.00	
1–3	132	29.2	113	26.2	1.29	0.94–1.75
4–9	43	9.5	34	7.9	1.09	0.96–1.23
>10	47	10.4	32	7.4	1.05	1.00–1.10
Unknown	25	(5.5)	54	(10.7)		
Metastases						
No	467	92.3	432	94.5	1.00	
Yes	39	7.7	25	5.5	1.44	0.86–2.43
Socio-demographic factors						
Marital Status						
Married	211	42.1	291	64.0	1.00	
Widow	118	23.6	86	18.9	1.89	1.36–2.63
Separate/divorced	127	25.4	52	11.4	3.37	2.33–4.87
Never married	45	9.0	26	5.7	2.39	1.43–3.99
Unknown	5	(1.0)	2	(0.4)		
Education						
<12 yr	172	41.4	54	13.9	1.00	
12 yr	118	28.4	129	33.1	0.29	0.19–0.43
>12 yr	126	30.3	207	53.1	0.19	0.13–0.28
Unknown	90	(17.8)	67	(14.7)		
Poverty index						
<126	155	42.2	31	8.7	1.00	
126–200	51	13.9	28	7.8	0.36	0.20–0.67
201–300	59	16.1	60	16.8	0.20	0.12–0.33
301–400	39	10.6	45	12.6	0.17	0.10–0.31
>400	63	17.2	194	54.2	0.06	0.04–0.11
Unknown	139	(27.4)	99	(21.6)		
Occupation						
Housewives	59	14.4	146	37.4	1.00	
Managerial/professional	62	15.1	106	27.2	1.45	0.94–2.24
Technical sales and administration	84	20.5	99	25.4	2.10	1.38–3.20
Service	154	37.6	24	6.2	15.90	9.38–26.90
Others	51	12.4	15	3.9	8.41	4.36–16.10
Unknown	96	(19.0)	67	14.6		
Host factors						
Body mass index[c]						
<20	36	8.1	53	12.7	1.00	
20.0–21.9	40	9.0	111	26.7	0.53	0.30–0.93
22.00–27.2	179	40.2	194	46.6	1.36	0.85–2.17
≥27.3	190	42.7	58	13.9	4.82	2.88–8.08
Unknown	61	(12.1)	41	(9.0)		

Table 2—Continued

Variables	Black (n = 506)		White (n = 457)		OR	95% CI
	n	%[a]	n	%		
Lifestyle						
Alcohol consumption						
Nondrinker	200	49.9	105	27.6	1.00	
<0.5 drinks/day	99	24.7	149	39.2	0.35	0.25–0.49
0.5–1.9 drinks/day	65	16.2	78	20.5	0.44	0.29–0.66
≥2 drinks/day	37	9.2	48	12.6	0.41	0.25–0.66
Unknown	105	(20.8)	77	(16.8)		
Smoking						
Never	212	51.2	200	51.2	1.00	
Ex-smoker	121	29.2	137	35.0	0.83	0.61–1.14
Current smoker	81	19.6	54	13.8	1.42	0.95–2.10
Unknown	92	(18.2)	66	(14.4)		
Reproductive experience						
Parity						
0	94	20.8	88	20.9	1.00	
1–2	183	40.4	190	45.1	0.90	0.63–1.29
3–4	97	21.4	121	28.7	0.75	0.51–1.11
≥5	79	17.4	22	5.2	3.36	1.93–5.86
Unknown	53	(10.5)	36	(7.9)		
Age at first pregnancy						
Never pregnant	110	23.6	97	22.5	1.00	
<20	176	37.8	63	14.6	2.46	1.66–3.66
≥20	180	38.6	271	62.9	0.59	0.42–0.82
Unknown	61	(12.1)	41	(9.0)		
Access to health care						
Usual source of care						
None	82	19.8	50	17.1	1.00	
Public Clinic	42	10.1	2	2.1	12.81	2.97–55.22
Private	291	70.1	339	80.8	0.52	0.36–0.77
Unknown	91	(18.0)	66	(14.4)		
Health insurance						
None	58	13.9	8	2.1	1.00	
Public (Medicare & Medicaid)	113	27.1	18	4.6	0.87	0.36–2.11
Private	246	59.0	365	93.4	0.09	0.04–0.20
Unknown	89	(17.6)	66	(14.4)		

[a] Percent of known response.
[b] Items in parentheses indicate the percentage of total.
[c] Body mass index calculated as (weight [kg]/height [m]^2); cutpoints were the 25th, 50th, and 85th percentile for women age 20–29 in the Second National Health and Nutrition Examination Survey, United States, 1976–1980 (United States Department of Health and Human Services, 1987)

socioeconomic strata because of very little overlap. Therefore, we chose a higher cutpoint of 400. White women of lower SES (poverty index ≤400) have a larger proportion of tumors of higher nuclear grade and higher mitotic activity, as well as a lesser proportion of tubular formation when compared with white women of higher SES level (Table 5). For white women, upper SES leads to significantly lower risk in the least favorable category of nuclear atypia (OR = 0.32), mitotic activity (OR = 0.41), grade (OR = 0.38) and necrosis (OR = 0.56), and a higher probability of marked tubular formation, a favorable category (OR = 1.50). These odds ratios remain significant after adjusting for age, stage, and location except for tubular formation.

The association of these histological parameters and SES shows a different pattern in black women. Lower SES is not found to be associated with less favorable tumors. For most of the tumor characteristics examined, there are no consistent patterns associated with poverty index. Furthermore, among black women, upper SES appears to be associated positively with histological parameters that are indicators of poor prognosis (Table 5). Black women of upper SES have higher proportions of grade 3 nuclear atypia (27%) than their black, lower SES counterparts (15.3%). The adjusted ORs for high mitotic activity and histological grade in upper SES black women are 1.4 and 1.6, respectively, relative to lower SES women. However, those findings are limited by the small number of black women ($n = 63$) in the high SES category. CIs for all the ORs are quite wide and all include one.

Discussion

Histological differences in breast carcinoma between blacks and whites have been hypothesized to play a role in the interracial survival differences. Studies have reported more aggressive and less favorable tumor types among black patients. Mohla *et al.* (15) evaluated cytosolic estrogen receptors, progesterone receptors, and tumor differentiation among 146 black women with breast cancer from one university hospital, but did not include any white patients for comparison. They reported significantly higher proportions of estrogen receptor-negative (42%) and poorly-differentiated (55.5%) tumors among the study subjects than those published previously for white patients. Ownby *et al.* (16) reviewed all cases entered into the Breast Cancer Prognostic Study in the Detroit area and observed that blacks were more likely to have high grade tumors than whites. Although this study used a standardized classification and

Table 3 Relative odds of specific tumor characteristics among black breast cancer patients compared with whites

Variables	Black		White		Crude		Adjusted[a]	
	n	%	*n*	%	OR	95% CI	OR	95% CI
Nuclear atypia								
1	153	30.7	218	47.8	1.00		1.00	
2	263	52.7	187	41.0	2.00	(1.52–2.65)	1.90	(1.42–2.55)
3	83	16.6	51	11.2	2.32	(1.55–3.47)	1.97	(1.27–3.04)
Mitotic activity								
1	249	50.6	291	64.7	1.00		1.00	
2	154	31.3	115	25.6	1.57	(1.17–2.10)	1.47	(1.08–2.00)
3	89	18.1	44	9.8	2.36	(1.59–3.52)	2.05	(1.34–3.14)
Tubular formation[b]								
None or few	377	77.6	266	63.9	1.00		1.00	
Moderate and well	109	22.4	150	36.1	0.51	(0.38–0.69)	0.57	(0.42–0.77)
Grade								
1	109	21.8	129	28.4	1.00		1.00	
2	295	59.0	262	57.7	1.33	(0.98–1.81)	1.19	(0.87–1.64)
3	96	19.2	63	13.9	1.80	(1.20–2.71)	1.58	(1.02–2.45)
Estrogen receptor								
Negative and border	185	44.5	143	36.7	1.00		1.00	
Positive	231	55.5	247	63.3	0.72	(0.55–0.96)	0.78	(0.58–1.05)
Blood vessel invasion								
No	432	87.3	393	86.9	1.00		1.00	
Yes	63	12.7	59	13.1	0.97	(0.66–1.42)	0.85	(0.57–1.29)
Lymphatic invasion								
No	405	81.7	375	82.8	1.00		1.00	
Yes	91	18.3	78	17.2	1.08	(0.77–1.51)	0.92	(0.64–1.33)
Necrosis								
No	239	48.1	269	59.5	1.00		1.00	
Yes	258	51.9	183	40.5	1.59	(1.23–2.05)	1.51	(1.16–1.98)
Fibrosis								
None and mild	167	33.4	106	23.4	1.00		1.00	
Moderate	223	44.6	233	51.3	0.61	(0.42–0.87)	0.59	(0.43–0.81)
Marked	110	22.0	115	25.3	0.61	(0.42–0.88)	0.65	(0.45–0.94)
Cell reaction to tumor								
None	89	17.8	106	23.4	1.00		1.00	
Mild	279	55.8	252	55.5	1.32	(0.95–1.83)	1.32	(0.95–1.89)
Moderate and marked	132	26.4	96	21.1	1.64	(1.12–2.41)	1.62	(1.06–2.48)

[a] Adjusted for age at diagnosis (20–49, 50–64, 65–79), stage (I, II (no), II (n1), III, IV), and metropolitan area (Atlanta, New Orleans, San Francisco/Oakland).
[b] Lobular carcinoma cases are excluded.

grading system for review by a panel of five pathologists and enrolled a large sample of white patients ($n = 1005$), only 73 black patients were included.

The design of the present study provides for a high degree of credibility of the evaluation of histological parameters because all slides were evaluated by an expert pathologist who was totally blinded with respect to the identification of patients, including race. In addition, the study is population based with samples of patients from three distinct geographic areas so that generalizations of the findings can be made. Other strengths include a large sample size, a very high percent of pathology review (90.4%), high response rate of in-person interview with patients (83%), assessment of stage by a single group using standardized criteria, direct determination of SES and other host and lifestyle factors from patient interview, and the availability of other confounding variables that were adjusted for in the analysis.

Although the strengths of the current study are apparent, there are some sources of bias. Residue confounding because of categorization of ordinal variables may result in incomplete adjustment. This may explain the residue differences in tumor characteristics among blacks and whites. An additional limitation is the lack of inclusion of other potential confounders that may be associated with tumor characteristics, such as family history of breast cancer, detailed use of oral contraceptives, or other exogenous estrogens.

In spite of the limitations, the present study represents the largest and most detailed analysis of breast carcinoma in black and white women to date that clearly documents a more aggressive tumor in blacks. Therefore, biological reasons should be explored to identify the causes of these findings: 1) Breast carcinomas in black women display tumor characteristics of poorer differentiation as compared with white women, namely, increased nuclear atypia and mitotic activity, higher grade, less tubule formation, and a higher percent of estrogen receptor negative tumors. 2) Host response to breast carcinomas is characterized by less fibrosis and more white blood cell infiltration in black than in white women. 3) Although in white women higher socioeconomic indicators are associated with better tumor differentiation, such a trend is not seen in black women. In fact, black women of higher socioeconomic stratum tend to have less differentiated tumors than their lower SES counterparts. 4) The B/W differences in the aforementioned tumor characteristics remain after adjusting for the following social and lifestyle factors: marital status, education, poverty index, occupation, body mass index, smoking, alcohol consumption, parity, age at first pregnancy, usual source of health care, and type of insurance coverage.

Therefore, the data lead to the suggestion that the carcinogenic insult to the target cell is more profound for black than for white women. The carcinogens specifically target-

Table 4 Relative odds of specific histological parameters among black breast cancer patients compared with whites adjusted for selected factors

Variables in model	Polychotomous ordinal logistic regression models						
	Nuclear atypia	Mitosis	Tubular formation	Grade	Estrogen receptor	Fibrosis	Necrosis
	n = 687 OR	n = 677 OR	*n* = 647 OR	*n* = 687 OR	*n* = 579 OR	*n* = 684 OR	n = 681 OR
Race	1.98 (1.49–2.64)	1.84 (1.37–2.48)	0.49 (0.35–0.70)	1.48 (1.10–1.98)	0.76 (0.54–1.06)	0.69 (0.52–0.92)	1.59 (1.18–2.16)
Race, design	1.77 (1.31–2.39)	1.72 (1.26–2.34)	0.55 (0.38–0.79)	1.34 (0.99–1.82)	0.81 (0.57–1.15)	0.71 (0.53–0.96)	1.60 (1.16–2.21)
Race, design, SES	1.93 (1.35–2.76)	1.89 (1.31–2.74)	0.50 (0.32–0.78)	1.56 (1.08–2.25)	0.74 (0.49–1.14)	0.69 (0.49–0.98)	1.45 (0.98–2.13)
Race, design, SES, host factor, lifestyle	1.83 (1.26–2.66)	1.84 (1.25–2.70)	0.46 (0.29–0.73)	1.42 (0.97–2.08)	0.68 (0.44–1.06)	0.70 (0.49–1.01)	1.42 (0.95–2.13)
Race, design, SES, host factor, lifestyle, reproductive experience	1.79 (1.23–2.62)	1.77 (1.20–2.62)	0.48 (0.30–0.78)	1.34 (0.91–1.97)	0.76 (0.48–1.19)	0.70 (0.48–1.01)	1.37 (0.90–2.06)
Race, design, host factor, lifestyle, reproductive experience, health care access	1.78 (1.21–2.62)	1.77 (1.19–2.63)	0.46 (0.29–0.75)	1.33 (0.90–1.97)	0.81 (0.51–1.29)	0.68 (0.47–0.99)	1.37 (0.90–2.08)

Design: stage, age at diagnosis, and metropolitan area; SES: marital status, education, poverty index, occupation; host factor: body mass index; lifestyle: smoking, alcohol consumption; reproductive experience: parity, age at first pregnancy; health care access: usual source of care, health insurance.

Table 5 Selected histological parameters by socioeconomic status among black and white breast cancer patients

Variables	Black						White					
	Higher SES[a]		Lower SES[b]		Crude OR (95%CI)	Adjusted[c] OR (95%CI)	Higher SES[a]		Lower SES[b]		Crude OR (95%CI)	Adjusted[c] OR (95%CI)
	n	%	*n*	%			*n*	%	*n*	%		
Nuclear atypia												
1	21	33.3	84	28.0	1.00	1.00	103	53.1	69	42.3	1.00	1.00
2	25	39.7	170	56.7	0.59 (0.31–1.11)	0.37 (0.18–0.75)	77	39.7	65	39.9	0.79 (0.51–1.24)	0.84 (0.51–1.38)
3	17	27.0	46	15.3	1.48 (0.71–3.08)	0.94 (0.40–2.19)	14	7.2	29	17.8	0.32 (0.16–0.66)	0.28 (0.13–0.61)
Mitotic activity												
1	28	45.2	144	49.0	1.00	1.00	131	69.0	92	56.4	1.00	1.00
2	17	27.4	101	34.4	0.87 (0.45–1.66)	0.68 (0.34–1.37)	45	23.7	47	28.8	0.67 (0.41–1.10)	0.72 (0.42–1.34)
3	17	27.4	49	16.7	1.78 (0.90–3.54)	1.41 (0.65–3.07)	14	7.4	24	14.7	0.41 (0.20–0.83)	0.36 (0.17–0.78)
Tubular formation												
None or few	47	77.1	232	78.1	1.00	1.00	105	59.7	100	69.0	1.00	1.00
Moderate and well	14	23.0	65	21.9	1.06 (0.55–2.05)	0.96 (0.48 –1.92)	71	40.3	45	31.0	1.50 (1.01–2.39)	1.41 (0.85–2.34)
Grade												
1	10	16.1	66	21.9	1.00	1.00	67	34.5	38	23.3	1.00	1.00
2	35	56.5	183	60.5	1.27 (0.60–2.70)	1.02 (0.45–2.33)	106	54.6	94	57.7	0.64 (0.39–1.03)	0.69 (0.40–1.17)
3	17	27.4	53	17.6	2.12 (0.90–5.01)	1.61 (0.63–4.13)	21	10.8	31	19.0	0.38 (0.19–.076)	0.31 (0.14–0.69)
Estrogen receptor												
Negative and border	24	49.0	108	43.5	1.00	1.00	59	36.2	59	40.4	1.00	1.00
Positive	25	51.0	140	56.5	0.80 (0.44–1.49)	0.86 (0.45–1.66)	104	63.8	87	59.6	1.20 (0.76–1.89)	1.54 (0.93–2.55)
Fibrosis												
None and mild	25	40.3	105	35.0	1.00	1.00	47	24.2	37	23.0	1.00	1.00
Moderate	25	40.3	134	44.7	0.78 (0.43–1.44)	0.79 (0.40–1.54)	98	50.5	87	54.0	0.89 (0.53–1.49)	1.03 (0.58–1.81)
Marked	12	19.4	61	20.3	0.83 (0.39–1.76)	0.75 (0.32–1.75)	49	25.3	37	23.0	1.04 (0.57–1.91)	1.22 (0.63–2.35)
Necrosis												
No	32	51.6	129	43.3	1.00	1.00	122	63.2	79	49.1	1.00	1.00
Yes	30	48.4	169	56.7	0.72 (0.41–1.24)	0.70 (0.39–1.25)	71	36.8	82	50.9	0.56 (0.37–0.86)	0.56 (0.35–0.91)

[a] Poverty index > 400.
[b] Poverty index ≤ 400.
[c] Adjusted for age at diagnosis, stage and metropolitan area (see footnotes in *Table* 3).

ing the human ductal breast epithelium have not been identified. Therefore, it is not possible to assess racial differences in their delivery. However, it seems clear that carcinogenesis in the human breast is a multistep, multifactorial process that evolves over many years. Recently proposed models of human carcinogenesis postulate that the invasive malignant cell is the product of an accumulation of molecular alterations, which in the case of colon carcinoma have been proposed to be at least six in number (26). It is clear that cancer cells contain a multiplicity of molecular alterations and it is possible that the amount and type of these alterations determine the degree of differentiation of the tumor. According to this model, it could be postulated that breast carcinomas in black women have a set of molecular abnor-

malities that may be different or somehow more advanced than in white women. This hypothesis could be tested when the set of molecular alterations pathognomonic of breast carcinoma become better defined. It also may become possible to link specific molecular alterations with specific environmental carcinogens.

The prevailing theory of breast carcinogenesis in humans assigns a dominant role to unopposed estrogenic stimulation. Estrogens stimulate the ductal epithelium and are therefore expected to increase the mitotic activity in the target cell. This could mean that the increased mitotic activity in breast carcinomas of black women indicates higher levels of circulating estrogens. To our knowledge, this has not been reported. However, Gilsanz *et al.* (27) reported a substantially greater increase in bone density in black girls than white girls during late puberty, suggesting interracial differences in hormonal production. Other mechanisms of increased proliferation could be invoked. The deletion or mutation of suppressor genes such as the *p53* and the retinoblastoma genes results in a loss of control of cell replication (28). Therefore, it could be postulated that the abnormalities in suppressor genes may be more advanced in black than in white women.

Most of the studies that led to the postulation of unopposed estrogen as the overriding factor in human breast carcinogenesis have been conducted in white women (29). One comerstone of the estrogen theory is the increased risk associated with a delayed first full term pregnancy (30). Black women, in general, tend to have the first full term pregnancy earlier than white women. It would appear at this point, however, that the higher grade of breast carcinomas in blacks is not explainable in terms of delay in the first full term pregnancy. But it remains probable that delayed first full term pregnancy affects the breast cancer risk in black women.

Although in normal conditions most of the estrogenic effects are derived from estradiol synthesized by the ovary, other substances and other sources may play a role. Alcohol intake has been reported to increase the risk of breast carcinoma (31). Alcohol consumption increases the levels of estrogens in the blood and urine, as well as their bioavailability (32). A positive association between breast cancer and blood levels of the insecticide metabolite 1,1-dichloro-2.2-bis-*p*-chlorophenyl has been reported (33). Dichlorodiphenyl-trichloroethane and its metabolites exert estrogenic effect (34) and accelerate mammary tumors in rats (35). It has been reported that dichlorodiphenyl-trichloroethane analogs may have estrogenic or antiestrogenic effect (36). Spraying of insecticides in homes has been reported more frequently by blacks than whites (37). Numerous compounds have been identified in edible vegetables and other environmental sources with both estrogenic and antiestrogenic effect; some plant estrogens can be excreted in considerable amounts in subjects on a vegetarian diet (38, 39). Tobacco smoking is also considered to have antiestrogenic effect (40).

Another possible explanation for our findings could be related to racial differences in the metabolism of carcinogens. Several recent investigations have pointed out racial differences in genotypes that determine the enzymes involved in the metabolism of carcinogens. It has been proposed that a high degree of activity of cytochrome P450-IID6 enzymes (measured with debrisoquine or other substrates) is associated with extensive conversion of procarcinogenic substances to ultimate carcinogens in tobacco smoke (41, 42). Blacks have a lower prevalence of poor metabolizers of debrisoquine than whites (43), which suggests that more extensive metabolism of procarcinogens in tobacco smoke may be related to higher lung cancer rates in blacks. Blacks were three times as likely as whites to have the allele *CYP-1A1-Msp1*, involved in the metabolic activation of aromatic hydrocarbons (44). Interracial differences in the allelic distribution of proto-oncogenes have been reported. American blacks have significantly higher frequency of the Eco RI-DNA component of the *c-myc* oncogene than whites (45). Similarly, the rare alleles of the Harvey-*ras* proto-oncogene are higher in blacks with lung cancer than in other groups (46). Other abnormalities suspected to be involved in carcinogenesis are cell surface glycoproteins in the Lewis antigen system, which may be involved in human gastric carcinogenesis (47). Gastric cancer incidence rates in American blacks are at least double those of whites. Lewis a–b– (negative) phenotype is three and one-half times more frequent in blacks than in whites, 22% *versus* 6% (48). Further research is indicated to determine if greater exposure to carcinogens or genetic susceptibility to more carcinogenic pathways of metabolism plays a role in the more aggressive behavior of breast carcinoma in black women.

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Mr. TOWNS. This hearing will be concluded, and thank you very much for your testimony. I must run and try to make the vote. As I indicated, the record will be held open for 10 days. We will submit questions for to you answer. We appreciate your patience and cooperation.

[Whereupon, at 4:35 p.m., the subcommittee adjourned, to reconvene subject to the call of the Chair.]

[Additional information submitted for the hearing record follows:]

QUESTIONS FROM HON. EDOLPHUS TOWNS AND ANSWERS FROM ROBERT S. SIEGEL

Dr. Robert S. Siegel
Interim Medical Director
Cancer Center at George Washington University Medical Center
2150 Pennsylvania Avenue, N.W., Suite 3–431
Washington, D.C. 20037

DEAR DR. SIEGEL:

I am writing to send you the follow up questions from our hearing yesterday. I am sorry that time did not allow these to be covered or clarified during the hearing. You may elaborate on your answers as you feel necessary.

1. Would you concur that early detection is important to breast cancer survival?

a. Would you concur that, generally, breast cancer in black women is diagnosed at a later stage than in white women?

2. What is the key to early detection?

a. If we improve access, will that reduce mortality?

b. What can be done to improve our detection techniques?

i. Could you give a rough sense of how much better screening mammography is today than it was a decade ago?

3. From your study, when you controlled for stage of diagnosis, were there still differences between breast cancer in black women and that in white women?

a. When you controlled for stage, did black women have a higher mortality rate than white women?

b. You identify specific biological characteristics that differ, such as "black women were significantly less likely to have breast cancer tumors which are 'estrogen receptor positive'". At present, do we know why black women should be more likely to have these distinct characteristics in their cancers?

c. These distinctions only applied to the probability of their occurrence in black or white women. Did you observe any characteristics in the cancers of black women that were never observed in the cancers of white women?

Please reply to the Subcommittee in writing by October 19, 1994.

Thank you for testifying yesterday. As you will have noticed from the enquiries you received afterwards, your testimony was illuminating to the Subcommittee's investigation of minority women and breast cancer. If you have any questions regarding this follow up, please contact Allen Hill at (202) 225–2548. I am,

Sincerely,

EDOLPHUS "ED" TOWNS
Chairman, Subcommittee on Human Resources and Intergovernmental Relations

The Honorable Edolphus Towns
Human Resources and Intergovernmental Relations Subcommittee
of the Committee on Government Operations

DEAR MR. TOWNS:

I appreciated the opportunity to testify before your committee on October 4. I would be pleased to answer the additional questions that you have forwarded to me.

1. I would concur that early detection is important in breast cancer survival. Our ability to cure patients with breast cancer has not substantially improved in the past 20 years. An individual woman's best opportunity for cure, should she develop breast cancer, is early diagnosis.

1a. Numerous studies (including our own) have concluded that in addition to having a more aggressive tumor biology, black women generally present for medical attention at a later stage. In our study of patients with stages I and II breast cancer, 41% of white women presented with stage II disease at diagnosis while 57% of black women presented with stage II disease at diagnosis.

2. The key to early detection in 1994 is to utilize the three methods of early breast cancer detection in an optimal way. Women ideally should be taught to do monthly

self-breast examination, should undergo a good clinical examination at least once per year (more often if clinically indicated) and should undergo mammography in accordance with a strategy planned with her primary care practitioner. In the absence of increased risk for breast cancer, I believe a woman should undergo a baseline mammogram prior to the age of 40, then have a mammogram once every one to two years between 40 and 50, and have annual mammograms after the age of 50.

2a. Limited access has been a problem for underserved women in black and white communities. Any program which improves access to clinical breast examination and mammography will ultimately will save lives. Individual women, of course, must make use of improved access in order to benefit.

2b. Improved detection techniques appear to be on the horizon. As was mentioned in the subcommittee hearing, new techniques using MRI scanning and ditigal mammography, as well as PET scanning all represent possible improvements in the sensitivity of screening mammography. I am also optimistic that blood tests that assess serum tumor marker levels will ultimately be useful for screening purposes. I believe mammography has improved in the past decade by providing clearer images of the breast tissue as well as decreasing the radiation exposure during the process. Mammography, however, continues to be plagued by its relative insensitivity in identifying early lesions in premenopausal women, especially those with dense breasts. In 1994, the false negative rate for mammography is 11% to 20%.

3. In our study, we found that black women with stage I breast cancer had slightly higher risk of premature death compared to white women, although the difference is not statistically significant at this time. For stage II breast cancer, black women clearly had diminished survival compared to white women.

3b. There were three pathologic characteristics in our study which identified more aggressive tumors in black women versus white women. The explanation for these apparent differences in pathology and biological aggressiveness is not known at this time.

3c. The focus of our review of breast pathology in both black and white populations was the likelihood of showing characteristics that conferred more aggressive biologic behavior. There were no pathologic characteristics (good or bad) seen in the tumors of black women that were not seen in the tumors of white women. In addition, a white woman with the same constellation of pathologic factors (such as estrogen receptor negative, high "S phase", and high tumor grade) had an equally diminished survival.

I hope these answers are clear and I would be happy to answer additional questions or further clarify my answers to these questions if you so request. In addition, I would be pleased to add further information at any time if I can be helpful.

Sincerely,

ROBERT S. SIEGEL, M.D.
Asociate Professor of Medicine
Division of Hematology and Oncology
Interim Medical Director, Cancer Center

QUESTIONS FROM HON. EDOLPHUS TOWNS AND ANSWERS FROM RICHARD M. ELLEDGE

Dr. Richard M. Elledge
Division of Oncology
University of Texas Health Science Center at San Antonio
7703 Floyd Curl Drive
San Antonio, Texas 78284–7884

DEAR DR. ELLEDGE:

I am writing to send you the follow up questions from our hearing yesterday. I am sorry that time did not allow these to be covered or clarified during the hearing. You may elaborate on your answers as you feel necessary.

1. Would you concur that early detection is important to breast cancer survival?

a. Would you concur that, generally, breast cancer in black women is diagnosed at a later stage than in white women?

b. In your study, was breast cancer diagnosed at a later stage in Hispanic women than in white women?

2. What is the key to early detection?

a. If we improve access, will that reduce mortality?

b. What can be done to improve our detection techniques?

i. Could you give a rough sense of how much better screening mammography is today than it was a decade ago?

3. In your study, when you controlled for stage of diagnosis, did you still observe differences between breast cancers in minority women and those in white women?

a. When you controlled for stage, did black women have a higher mortality rate than white women?

b. When you controlled for stage, did Hispanic women have a higher mortality rate than white women?

c. After you controlled for stage, what other differences did you observe?

d. Is it your view that if enough patient and tumor characteristics are used (your testimony refers to age, menopausal status, tumor size, et cetera), then the treatment decisions can be made independent of patient ethnicity?

i. Does this imply that if all these factors are taken into account and treatment controlled for, the mortality rates should be the same for black and white women? If not, why not?

(1) Do you know if this has been studied, and, if so, do such studies confirm this?

Please reply to the Subcommittee in writing by October 19, 1994.

Thank you for testifying yesterday. As you will have noticed from the enquiries you received afterwards, your testimony was illuminating to the Subcommittee's investigation of minority women and breast cancer. If you have any questions regarding this follow up, please contact Allen Hill at (202) 225–2548. I am,

Sincerely,

EDOLPHUS "ED" TOWNS

Chairman, Subcommittee on Human Resources and Intergovernmental Relations

MEMORANDUM

Date: October 10, 1994
To: Allen Hill
From: Richard Elledge, M.D.
Subject: Reply to Questions on Minority Women and Breast Cancer

1) Early detection is the key to improving survival in all women with breast cancer. Black women with breast cancer are diagnosed at a later stage. In our study, Hispanic women were diagnosed at a later stage than white women.

2) Women should be educated about the importance of screening mammography. Improvement in access is important and this could be achieved by a lowering of financial and logistical barriers. Though not proven in randomized trials to decrease mortality, women should receive thorough and complete instructions on breast self exam. Improving access while simultaneously improving attitudes towards early detection measures will reduce mortality.

3) When controlling for stage at presentation, blacks but not hispanics had a higher mortality within each stage.

After taking into consideration other factors such as menopausal status, age, tumor size, nodal status, histologic grade, ER status, and proliferative fraction, ethnicity adds little, if any, independent information to the therapeutic decision making process, and should not be used. This applies to making treatment decisions for individual patients. In a statistical model, after we controlled for tumor size, nodal status, age, and ER status, blacks had a relative risk of dying compared to whites of 1.2. While this was statistically significant, its clinical significance is small. If we would have been able to insert information on proliferative status and histologic grade into the model, I strongly suspect that even this small difference in adjusted relative risk would have disappeared, and there would have been no difference. This does not mean, however, that delay in diagnosis is not a contributing factor to the higher stage at diagnosis and worse mortality in minority breast cancer patients. In fact, I believe it is a substantial contributing factor.

The percentage of minority women receiving hormonal or systemic treatment is similar to whites.

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